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AMERICAN JOURNAL OF OPHTHALMOLOGY

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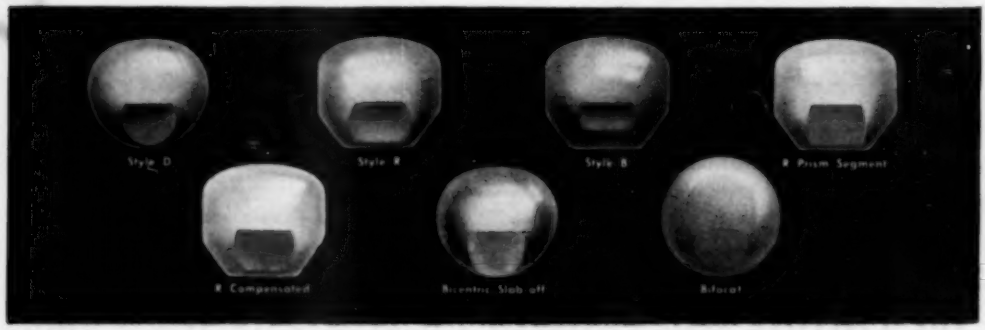

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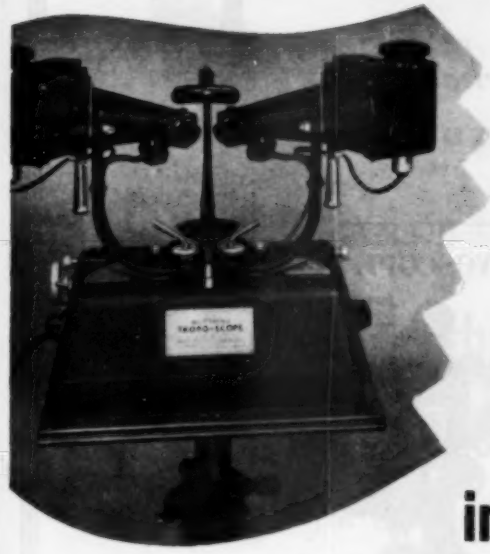

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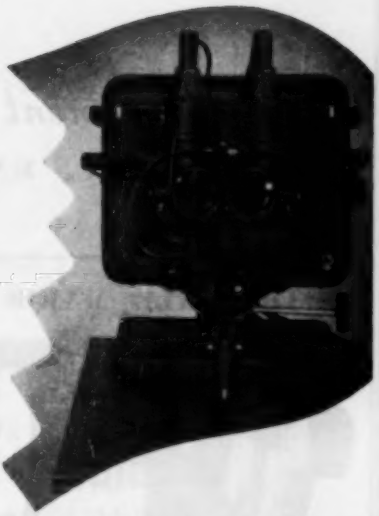

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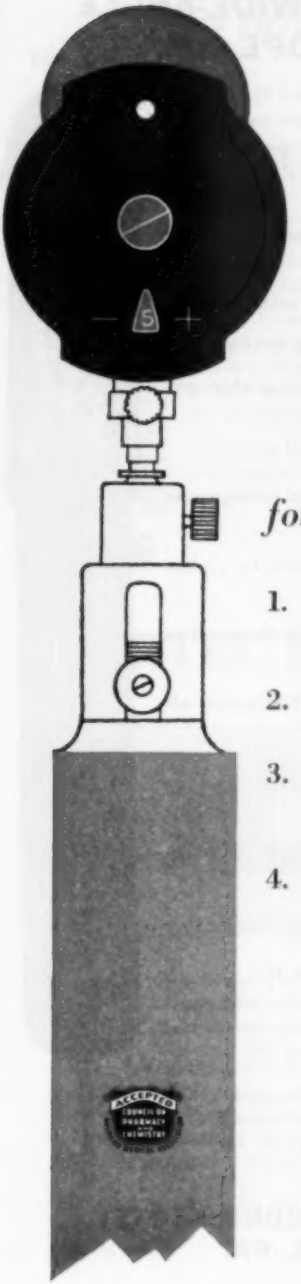

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ABSTRACTS

Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Retina and vitreous; Optic nerve and chiasm; Neuro-ophthalmology; Eyeball, orbit, sinuses; Eyelids, lacrimal apparatus; Tumors; Injuries; Systemic disease and parasites; Congenital deformities, heredity; Hygiene, sociology, education, and history 1166

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VOLUME 33 JULY, 1950 NUMBER 7

METASTATIC CARCINOMA OF THE EYE*

JAMES N. GREEAR, JR.,† M.D.
Washington, D.C.

The secondary tumor most often encountered in the eye is metastatic carcinoma; nonetheless it is rare and only occasionally reported. It has been pointed out that this tumor is far more frequent than references in the literature would indicate, since patients with cancer are not systematically examined for ocular involvement. It is generally conceded that many metastatic eye lesions are overlooked, for some are located paracentrally and develop slowly, and in numerous instances the general condition of the patient is so grave that eye disturbances pass unnoticed.

Since visual disturbances are the usual symptoms of ocular metastasis, practically all cases of metastatic carcinoma of the eye have been reported by ophthalmologists, but only a few have contributed more than one case. The estimated frequency, as reported from ophthalmic clinics, varies from 1 in 35,000 (Payne,[1] 1932) to 1 in 150,000 (Sattler,[2] 1926). Michail[3] (1932) examined 48,000 eyes microscopically, and found only one with metastatic carcinoma.

Reference to texts in general pathology would lead to the impression that secondary carcinoma of the eye is of little significance; at least it is not discussed. The few studies of the condition and reviews of the rather scant literature have resulted in reports chiefly statistical in nature, with emphasis on the site of the primary tumor rather than on the specific location of the ocular metastasis. Godtfredsen[4] made a study of the eyes of a large group of patients at the Radium Centre and Eye Clinic of the Finsen Institute in Copenhagen. All patients with any eye complaint were examined and, in addition, systematic examinations were made of the eyes of patients with tumors of the lung. Secondary carcinoma of the eye proved to be more frequent than had previously been supposed.

In Godtfredsen's series based on a group of patients in Denmark, metastatic carcinoma of the eye occurred one third to one half as frequently as primary malignant tumors in the choroid (malignant melanoma). His study showed, furthermore, that tumors in the lung gave rise to metastasis to the choroid just as often as did mammary carcinomas, although the latter were about 10 times as prevalent.

Figures in support of Godtfredsen's observations were reported by Baker[5] (1942) in a series of intracranial metastatic carcinomas. In 45 percent, the primary tumor was in the breast, in 45 percent in the lung, and in 10 percent in other locations.

The first case of ocular metastatic carcinoma recorded in the literature was that of Perls[6] (1872). The eyes of a man, 43 years of age, who had primary tumor of the lung, were examined post mortem and metastatic lesions of the choroid were demonstrated in each eye. Perls was of the opinion that there had been emboli of cancer cells into the choriocapillaris of each eye.

From the time of Perls's report until

* From the Registry of Ophthalmic Pathology, Armed Forces Institute of Pathology. Read before the Section on Ophthalmology, College of Physicians of Philadelphia, April, 1949.

† Consultant in Ophthalmology to the Office of the Surgeon General.

Fig. 1 (Greear). Intraduct adenocarcinoma of the breast (AFIP Acc. 197511).

1933, Ask[7] was able to collect 211 cases from the literature. Of this number, 152 were verified by pathologic examination, while 59 were diagnosed clinically. The primary tumor was identified in 127 cases. Although no effort has been made to search the literature for additional cases, it may be assumed that approximately 300 cases of metastatic carcinoma of the eye have been reported to date.

The most frequent site for metastatic lesions of the eye is the choroid, usually in the posterior pole of the eye and on the temporal side of the disc, at the point of entry of most of the posterior ciliary arteries. However, carcinoma may involve other structures of the eye, particularly the ciliary body, the iris, and the optic nerve. A wide distribution of secondary carcinoma in the uveal tract is demonstrated by cases from the collection of the Registry of Ophthalmic Pathology. Several of these selected for brief review illustrate metastatic carcinoma in parts of the eye seldom involved and choroidal metastasis with unusual features.

Report of cases

Case 1

One case (AFIP Acc. 197511) which recently came under my care is worthy of discussion in greater detail. The patient was a white woman aged 40 years, whose breast had been amputated one-and-one-half years previously for adenocarcinoma (fig. 1). About one year later frequent headaches first occurred, especially in and around the left eye, and gradually increased in severity. Headache had become constant and was more severe at night.

The right eye was normal in appearance. The left eye showed a mild ciliary blush, with congestion of the anterior ciliary vessels over the lower temporal quadrant of the globe. The base of the iris was pushed forward from the 3- to 6-o'clock positions. Between the 3- and 4-o'clock positions, a whitish gray mass which gave the impression of being in contact with the posterior surface of the cornea protruded from the iris angle. At the 6-o'clock position there was a similar mass. Between these two areas the iris angle was filled with tissue containing new blood vessels. During the next three weeks several new, mushroomlike masses appeared protruding from the iris angle into the anterior chamber between the 3- and 6-o'clock positions (fig. 3). The only change noted in the fundus was a flat detachment of

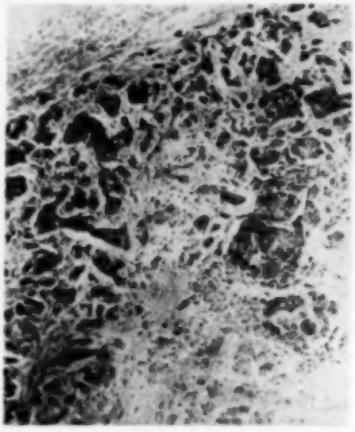

Fig. 2 (Greear). Metastatic adenocarcinoma, skin of chest wall, from same case as shown in Figure 1.

the retina in the periphery below and temporally.

Because of persistent pain the left eye was enucleated three weeks following the first examination.

On transillumination of the eye after enucleation, a shadow was projected from the equator to the root of the iris in the lower temporal field. Upon opening the globe, just anterior to the equator on the lower temporal side, the ciliary body was diffusely

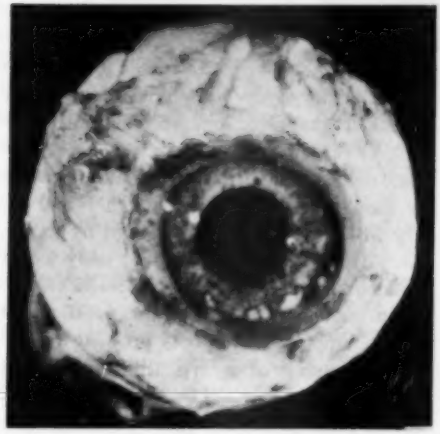

Fig. 3 (Greear). Metastatic adenocarcinoma, left eye, in anterior chamber angle from the 3- to 6-o'clock positions, from same case as Figures 1 and 2.

thickened, pushing the root of the iris forward (fig. 4). Whitish nodules projected from the inner surface of the ciliary body. Beginning at the ora serrata, a considerable portion of the lower temporal quadrant of the retina was detached, with gelatinous exudate in the subretinal space.

Microscopic examination of the tumor revealed nests and solid sheets of closely packed cells with hyperchromatic nuclei and scant cytoplasm. These had infiltrated the ciliary body and into the chamber angle anteriorly and also extended back to involve the anterior choroid. At the equator opposite the main tumor, another small mass of cells similar to those described was seen in the

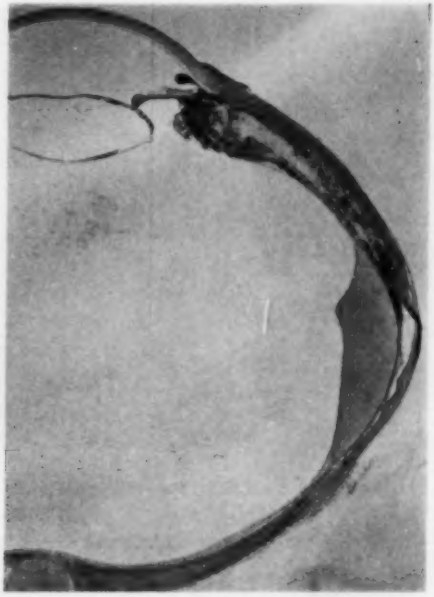

Fig. 4 (Greear). Metastatic adenocarcinoma of ciliary body with extension into anterior choroid and into angle of anterior chamber, from same case as Figures 1, 2, and 3.

choroid. Many of the tumor nodules had an abundant connective-tissue stroma and necrotic centers. The protrusion of tumor nodules from the ciliary body into the anterior

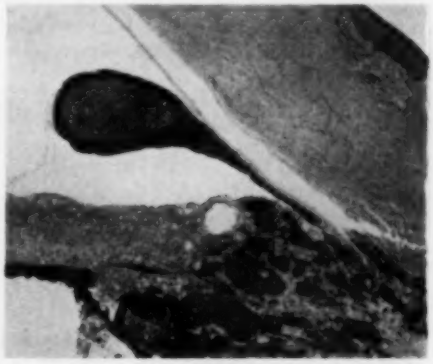

Fig. 5 (Greear). Pedunculated mass of tumor cells extending from ciliary body into anterior chamber angle, from same case as Figures 1, 2, 3, and 4.

Fig. 6 (Greear). Metastatic carcinoma of choroid ciliary body, and iris (AFIP Acc. 1119499).

chamber through the angle (fig. 5) produced a most unusual picture and might well serve as a guide to diagnosis.

The tumor of the breast was characterized by well-formed tubules and acini, while the metastatic lesion in the eye consisted of solid nests and sheets of cells. In reference to this variation in type between the metastatic lesion and the primary tumor, Willis,[8] in his recently published textbook, *The Pathology of Tumours* (1948), stated that "a single tumour may show a great variety of structure. Thus a cancer of the breast may contain areas of cribriform intraductal carcinoma, papillary growths, infiltrating adenocarcinoma, and polyhedral cell carcinoma, partly of 'medullary' and partly of 'scirrhous' type." Morphologic differences between the metastatic lesion and the primary tumor are as well recognized by pathologists as the complex pattern of the primary tumor.

Case 2

The ciliary body was the structure most extensively involved in a second case (AFIP Acc. 119499) in which there was also a separate metastasis to the choroid at the equator on the same side of the eye (figs. 6 and 7). The filtration angle was occluded by extension of the tumor of the ciliary body which invaded the ciliary zone of the iris.

On the opposite side of the pupil was a small clump of tumor cells growing on the anterior surface of the iris. It is possible that these cells were carried by the blood stream, but the location would suggest that they were engrafted on the surface of the iris.

Case 3 (AFIP Acc. 82616)

Probably no more than six proven metastatic carcinomas of the iris without other involvement of the eye have been reported. An excellent example from the Registry series is typical of the lesion in this structure. The iris on the nasal and lower quadrant was replaced by carcinomatous tissue (fig. 8). The eye was enucleated because of pain from secondary glaucoma. The patient died four months later from

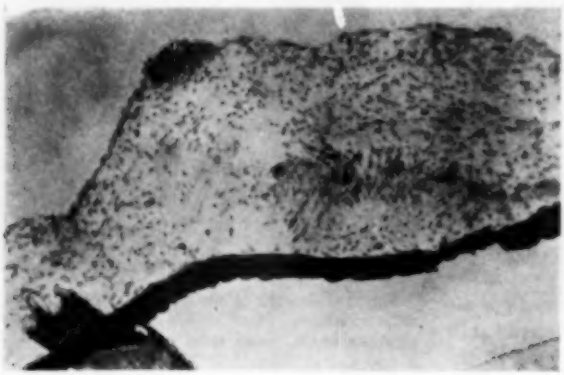

Fig. 7 (Greear). High-power view of iris lesion, from same case as Figure 6.

Fig. 8 (Greear). Metastatic carcinoma of iris with occlusion of chamber angle (AFIP Acc. 82616).

generalized carcinomatosis from a primary tumor in the lung.

Three of the cases (AFIP Acc. 81119, 81665, 69650) reviewed were examples of invasion of the nervehead by extension of metastatic carcinoma of the choroid (figs. 9 and 10). In two instances the tumor cells had invaded the retina, which is rarely involved, even secondarily. In a section from one specimen, a few tumor cells were seen posterior to the lamina cribrosa.

In another case (fig. 11) (AFIP Acc. 57689) the metastatic tumor appeared to be primary in the optic nerve and to have extended into the nervehead and thence to the choroid, thus following in reverse order the course of extension in the three preceding cases.

Metastatic carcinoma which involves the optic nerve primarily is so seldom observed that this case and the case reviewed here is worthy of special mention even though it has already been reported by McDannald and Payne.[9]

CASE 4

The patient was a white woman, aged 42 years. Ophthalmoscopic examination revealed a light gray, slightly elevated mass at the temporal side of the disc and continuous with it. The eye was enucleated because of pain. The optic nerve measured seven mm. in diameter just behind the eye. The nerve fibers were replaced by tumor cells. The new growth penetrated the cribriform plate and involved the disc by replacing the nerve fibers in a tuftlike arrangement, giving the appearance of papilledema. Reese, in commenting on this case, said that he was convinced that the carcinoma had metastasized first to the optic nerve and that the choroidal involvement resulted from extension.

CASE 5

In another case (AFIP Acc. 93725) there was epibulbar metastasis (fig. 12) from an

Fig. 9 (Greear). Metastatic carcinoma of choroid with invasion of nervehead (AFIP Acc. 81665).

Fig. 10 (Greear). Metastatic carcinoma of choroid with invasion of retina and optic nerve posterior to lamina cribrosa (AFIP Acc. 69650).

adenocarcinoma of the breast. The tumor cells had penetrated the sclera along a posterior ciliary artery from the metastatic lesion, but none had yet reached the interior of the eye. Extension of metastatic carcinoma of the orbit into the eye by way of the vessels is rarely observed.

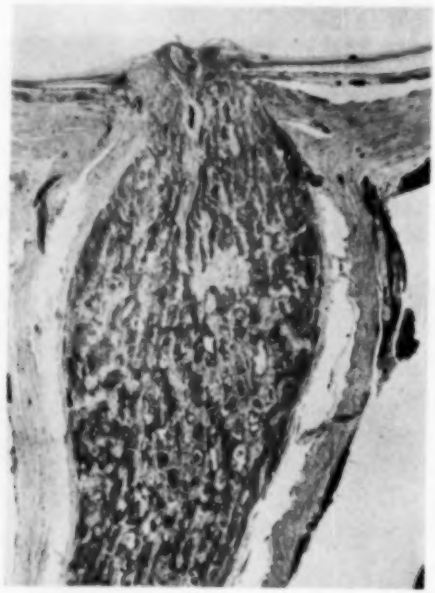

Fig. 11 (Greear). Carcinoma metastatic in optic nerve invading the choroid (AFIP Acc. 57689).

Case 6

Three separate, unconnected masses of tumor cells could be seen in the choroid in another case (AFIP Acc. 159525) (fig. 13). Each of these masses was flat and extended laterally in typical fashion. The fact that three lesions, apparently at the same stage of development, were present in the same eye would strengthen the belief that a shower of emboli accounted for their implantation.

Case 7

Metastatic carcinoma of the choroid in another instance (AFIP Acc. 111881) (fig. 14) has taken on an unusual configuration and has protruded into the space normally occupied by the vitreous.

Case 8

In still another unusual example (AFIP Acc. 36871), the choroidal metastasis from a primary carcinoma of the lung has perforated Bruch's membrane (fig. 15) and

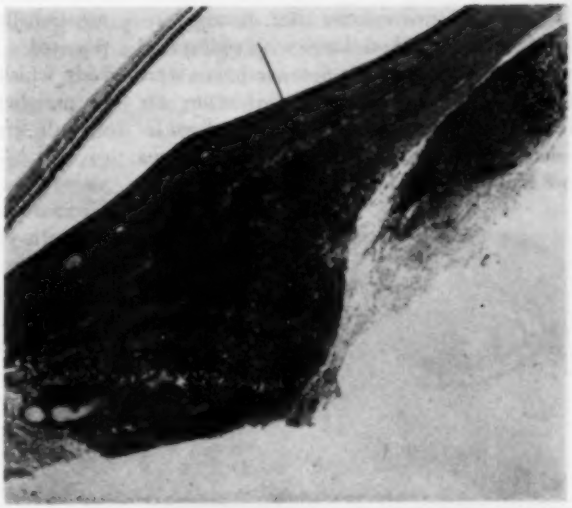

Fig. 12 (Greear). Epibulbar metastatic carcinoma invading sclera along emissary canal (AFIP Acc. 93725).

grown rapidly into the subretinal space. The carcinoma of the lung was not discovered until after the choroidal tumor was identified microscopically as a metastatic lesion. Rupture of Bruch's membrane by metastatic carcinoma of the choroid, as noted in this instance, is rare. The tumor tends to spread laterally because it meets with less resistance as it extends between the layers of the choroidal stroma. Malignant melanoma of the choroid, on the other hand, commonly breaks through Bruch's membrane.

Review of Literature

Another metastatic carcinoma of the choroid, interesting from the point of view of diagnosis, was first reported by Wilder.[10] The initial symptom of a 33-year-old white soldier was dimness of vision in the right eye. A tumor of the eye was seen on ophthalmoscopic examination and roentgenograms then revealed lesions of the lungs and bones.

Changes appeared in the left fundus 10 months after the original symptoms, and the

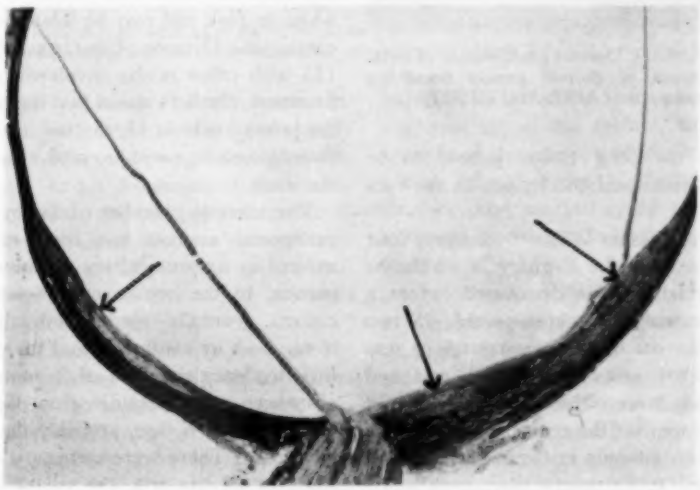

Fig. 13 (Greear). Three separate contemporary lesions of metastatic carcinoma in choroid (AFIP Acc. 159525).

patient died two months later. Autopsy revealed tumors of both lungs with widespread metastasis. Because the first symptoms were in the eye, it had been regarded as the site of the primary tumor and the generalized lesions as metastatic from malignant melanoma of the choroid. However, on histologic examination the lung tumor proved to be adenocarcinoma and the lesions in the eyes metastatic.

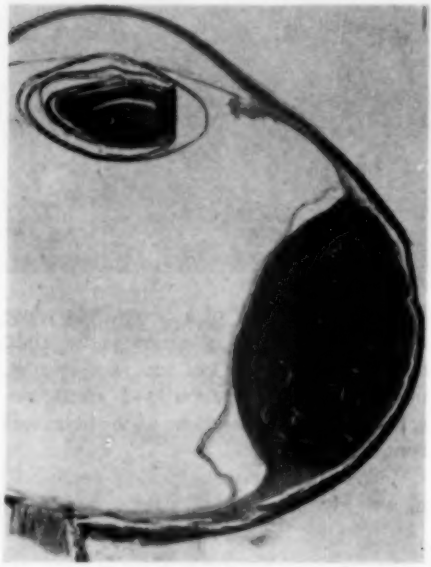

Fig. 14 (Greear). Unusual configuration of metastatic carcinoma of choroid grossly resembling malignant melanoma (AFIP Acc. 111881).

In her discussion Wilder[10] mentions four other cases from the Registry in which the ocular metastasis was discovered before a primary carcinoma was suspected; in two of these the site of the primary tumor was the lung. Forty-one of the 44 cases reviewed in this study were included in her series. In the largest number the ocular carcinoma was secondary to a tumor in the breast with the lung second as a primary site.

Examples of metastatic carcinoma of the eye in structures other than the choroid are occasionally found in the literature. Knapp[11] reported a metastatic tumor of the ciliary body which had pushed the iris away from its peripheric attachment. The growth was whitish gray and highly vascular; it was covered by a flaky white material which in places was massed in the form of balls. Microscopically, these proved to be tumor cells. In Knapp's opinion, isolated metastasis in the ciliary body or iris without involvement of the choroid is most unusual.

Duke-Elder[12] stated the same view even more emphatically and referred to metastatic carcinoma of the ciliary body as a "pathological curiosity" with no distinguishing diagnostic features. However, the whitish mushroomlike protrusions seen in the case discussed at length in this series and the ball-like nodules described by Knapp may constitute a distinctive feature.

Sanders[13] reported a case of metastatic carcinoma of the iris in which there was no involvement elsewhere in the uvea, the fourth of its kind in the literature at that time. In his opinion, metastatic carcinoma of the iris should be suspected in the presence of a discrete nodule in the stroma of the iris, usually near the pupil. The nodule is generally white or pink and may be lobulated. In discussing the 17 cases of metastasis to the iris (13 with other ocular involvement) in the literature, Sanders stated that the breast was the primary site in 11, thyroid in two, bronchus, stomach, prostate, and esophagus in one each.

The anterior chamber of the eyes of experimental animals has been successfully utilized as a tissue-culture medium for neoplasms. In the human eye, metastatic carcinoma generally spreads laterally in the uveal tract by continuity and the cells show little tendency to break off, become attached elsewhere, and continue to grow. Goldsmith[14] reported such a case, probably the only one on record. There were metastatic lesions in the root of the iris, the ciliary body, the choroid, and the sclera, and carcinomatous masses free in the anterior chamber. In this

instance secondary carcinoma was growing in the anterior chamber in the manner of a tissue culture.

Davis[15] reported a metastatic carcinoma of the optic disc. He remarked on the ophthalmoscopic resemblance of the lesion to papilledema. There is no doubt but that the ophthalmoscopic appearance of the lesions involving the optic nerve, which have already been described, would present a similar clinical picture. In his discussion of the mechanism of metastasis he recalled that von Recklinghausen had been the first to emphasize that retrograde extension is a frequent means of the spread of cancer, especially in organs having a venous pulse.

Smoleroff and Agatston[16] reported the only case on record of metastatic carcinoma involving the retina alone in the eye. As previously mentioned, two cases in the series from the Registry show invasion of the retina adjacent to the nervehead by extension from the optic nerve.

De Long[17] drew attention to the manner of growth of metastatic carcinoma of the choroid, laterally between the planes of the choroidal stroma, causing minimal thickening. This results in a fairly typical ophthalmoscopic appearance, as Duke-Elder[12] has pointed out. In his opinion the diagnosis of metastatic carcinoma of the choroid might be based on such features as the pale gray coloring, mottling of the surface, and indistinct borders of the lesion, and its flatness, which causes only a degree of thickening of the choroid, most marked at the posterior pole. Anterior retinal detachment may be an added feature.

Fig. 15 (Grecar). Unusual example of metastatic carcinoma of choroid breaking through Bruch's membrane and clinically resembling malignant melanoma (AFIP Acc. 36871).

Discussion

It has been emphasized that carcinoma, in general, metastasizes by way of the lymphatics. It is also true that certain carcinomas have a tendency to metastasize by way of the blood stream. However, toward the terminal stages of malignant disease of any type metastasis is more often blood borne.

When metastasis to the eye occurs, the primary lesion is usually located in the breast

or lung, and in these cases it is simple to postulate the mechanism of metastasis. However, in a significant number of cases, the primary tumor is found in the abdomen. In cerebral, as well as ocular metastasis, it has sometimes been noted that there is no evidence of pulmonary involvement. It is generally accepted that remote metastasis takes place through the blood stream, emboli lodging in smaller arterioles or capillaries. Some authors have advanced the view that individual tumor cells may pass through pulmonary capillaries and then on to the brain or structures of the eye.

Batson[18] has suggested a different mechanism for the production of metastatic lesions of structures within the cranial cavity. He based his views on post-mortem injections of the human venous system and on experiments with animals. He demonstrated a set of valveless, plexiform, longitudinal venous channels which join the cranial venous sinuses to the pelvic veins without mediation of the lungs. The "vertebral system of veins" carries the blood at low pressures, and the direction of flow is subject to arrests and reversals. These vessels are of particular significance during compression of the chest and abdomen in coughing, lifting, and straining. It is conceivable that sufficient increase in thoracic and abdominal pressure might produce a reversal in the sinuses of the brain which might be transmitted to the vessels of the eye.

The usual life span following the observation of metastatic lesions in the eye is between six months and one year; the average is approximately seven months. Therefore, it is evident that metastatic carcinoma involving the eye is a late manifestation, probably indicative of generalized carcinomatosis. Major surgical procedures should be avoided whenever possible, once metastatic lesions of the eye have been diagnosed. Furthermore, radical procedures for the removal of the primary carcinoma should not be undertaken until the eyes have been studied for ocular involvement indicating that generalized carcinomatosis has already occurred. The presence of an intraocular tumor demands that a careful survey be instituted for evidence of a primary lesion elsewhere. If the eye lesion proves to be secondary, operation should not be resorted to except for relief of pain.

When severe pain is not a factor, Lemoine and McLeod[19] have demonstrated that useful vision may be retained, even when both eyes are involved, by employing X-ray therapy to the metastatic tumors of the choroid. They reported a case of bilateral metastatic carcinoma of the choroid with detachment of both retinas. Following X-ray therapy, there was re-attachment of the retina in one eye, resulting in useful vision until the death of the patient.

Summary

Recent studies of groups of patients under treatment for carcinoma indicate that metastasis to the eye is more frequent than previously supposed, and, further, that metastatic lesions in the eye are relatively far more frequent from primary carcinoma of the lung than of the breast.

A review of a series of ocular metastatic carcinomas in the collection of the Registry of Ophthalmic Pathology demonstrates that lesions involve the ciliary body, the iris, the optic nerve, the sclera, and the retina, as well as the choroid.

The grayish white nodules seen in the angle of the anterior chamber in metastatic carcinoma of the ciliary body may be of diagnostic significance.

The eyes of patients with primary carcinoma of the lung or breast should always be carefully examined for metastatic lesions.

Metastatic carcinoma in the eyes is an indication that generalized carcinomatosis has already occurred. Therefore radical surgical procedures or enucleation should only be performed for relief of pain.

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REFERENCES

1. Payne, B. F.: Common intraocular tumors. Texas State J. Med., **28**:227-231, 1932.
2. Sattler, H.: Die bösartigen Geschwülste der Auges. Leipzig, S. Hirzel, 1926.
3. Michail, D.: Metastatic carcinoma of orbit. Brit. J. Ophth., **16**:537-545, 1932.
4. Godtfredsen, E.: The frequency of secondary carcinomas in the choroid. Acta ophth., **22**:394-400, 1944.
5. Baker, A. B.: Metastatic tumors of the nervous system. Arch. Path., **34**:495-537, 1942.
6. Perls, M.: Beiträge zur Geschwulstlehre. Virchows Arch. f. path. Anat., **56**:437-467, 1872.
7. Ask, O.: Zur Kenntnis des metastatischen Uvealkarzinoms. Acta ophth., **12**:308-347, 1934.
8. Willis, R. A.: The Pathology of Tumours, St. Louis, Mosby, 1948.
9. McDannald, C. E., and Payne, B. F.: Metastatic carcinoma of the optic nerve and choroid. Arch. Ophth., **12**:86-92, 1934.
10. Wilder, H. C.: Intraocular tumors in soldiers. World War II. Mil. Surgeon, **99**:459-490, 1946.
11. Knapp, A.: Metastatic carcinoma of the ciliary body. Arch. Ophth., **1**:604-608, 1929.
12. Duke-Elder, W. S.: Textbook of Ophthalmology. St. Louis, Mosby, 1940, v. 3, pp. 2520-2533.
13. Sanders, T. E.: Metastatic carcinoma of the iris. Am. J. Ophth., **21**:646-651, 1938.
14. Goldsmith, A. J. B.: Secondary carcinoma in the anterior chamber. Brit. J. Ophth., **29**:136-141, 1945.
15. Davis, W. T.: Metastatic carcinoma of the optic disk with report of a case. Arch. Ophth., **8**: 226-237, 1932.
16. Smoleroff, J. W., and Agatston, S. A.: Metastatic carcinoma of the retina; report of a case with pathologic observations. Arch. Ophth., **12**:359-365, 1934.
17. De Long, P.: Metastatic carcinoma of the choroid, report of a case. Am. J. Ophth., **16**:712-715, 1933.
18. Batson, O. V.: The function of the vertebral veins and their role in the spread of metastasis. Ann. Surg., **112**:138-149, 1940.
19. Lemoine, A. N., and McLeod, J.: Bilateral metastatic carcinoma of the choroid; successful roentgen treatment of one eye. Arch. Ophth., **16**:804-821, 1936.

THERAPEUTIC EXPERIMENTS IN ENDOPHTHALMITIS*

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Therapy is a most gratifying field of medicine. It can be developed to a true art by individual skill and adequate medicines. However, there are still some diseases of the eye, the therapy of which seems an insoluble problem; for example, metastatic abscesses of one or both of the vitreous bodies in septicemia, or purulent inflammation resisting every therapy after the penetration of foreign bodies into the eye. Occasionally, uneventful operation of a cataract may be followed by infection which may represent a difficult problem.

The therapy of endophthalmitis—irrespective of its posttraumatic, postoperative, or metastatic origin—has been inefficient. Formerly, there was no efficacious drug upon which the ophthalmologist could rely to save the eye. In cases of endophthalmia metastatica the patient's life might also be lost. In the words of Axenfeld, "the basic disease giving rise to a bilateral eye process is fatal in 85 percent of all cases."

The sulfonamides brought a revolutionary change in the treatment of this condition, and, since the advent of penicillin, it may be fairly stated that these processes no longer jeopardize a life. On the other hand, the sight of the diseased eye cannot always be saved even by penicillin therapy.

Case 1. A woman, aged 48 years, developed septicemia which started from a whitlow. Bronchopneumonia, meningitis, and bilateral abscess of the vitreous followed. Despite the fact that she was given 2,000,000 units of penicillin daily, chemosis and protrusion ensued.

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One week after the onset of the eye lesion, 0.5 cc. of the exudate was withdrawn from each eye, and the same quantity of penicillin was injected into the abscess. This procedure was repeated one week later. Both chambers became clear, deeper, and the chemosis ceased, but the eyeballs became soft, the lenses gray, and light perception ceased. (Observed at St. John's Hospital, Budapest.)

The penicillin directly injected into the vitreous brought about regression of the acute inflammatory symptoms and relief from pain, although vision was lost. Clinical and experimental data alike have shown that the injection of penicillin into the vitreous body is not free from risk. According to von Sallmann, Meyer, and Di Grandi, penicillin applied by this route may give rise to a mild retinitis, or, in severe cases to a circumscribed atrophy of the retina. Repeated injections frequently result in permanent damage to the retina and lens. The experiments of Leopold, Wiley, and Dennis on rabbits have shown that the same applies to streptomycin.

Case 2. A man, aged 72 years, had an intracapsular cataract extraction with round pupil. In 24 hours postoperatively endophthalmitis and panophthalmitis (pneumococcus) developed. Massive doses of sulfonamide were administered, 100,000 units of penicillin were injected intramuscularly, the prolapsed suppurating parts were removed, and the chamber was irrigated with two cc. of penicillin. On the next day this treatment was repeated. By the third day, the eye was painless but shrunken. One month later enucleation was performed. (Observed at St. John's Hospital.)

Although energetic local and general treatment was immediately started, the virulent infection resulted in destruction of the eye. Nevertheless, a new advantage of penicillin administration could be observed: in contrast to the painful suppurations observed in similar cases in the old days, the atrophy of the eyeball was painless. If the postoperative infection is due to a less virulent agent, penicillin may save the eye, as stated by Sorsby, Parry, Laszlo, and Penistan, as well as by van Heuven who successfully treated postoperative infections by irrigation of the infected chamber with penicillin.

Dunnington and von Sallmann observed purulent endophthalmitis after trephining operations and applied penicillin by iontophoresis (the positive electrode was placed upon the cornea, the negative one upon the neck); the eye became clear.

Roenne and Weizenblatt injected penicillin, in similar cases, into the vitreous with satisfactory results. Sorsby and Ungar claim that intraocular infections should in any case be treated as early as possible. The best result may be expected from the subconjunctival administration of penicillin, 50,000 units every six hours at least for the first 24 hours and, if possible, for 72 hours to guard against recurrence.

Case 3. The eye of a man, aged 21 years, was perforated by a piece of iron. He was immediately admitted to the eye department. In addition to the usual local treatment, 1,000,000 units of penicillin were administered intramuscularly. No endophthalmitis or panophthalmitis developed.

After dismissal he received out-patient treatment in the eye department: for two days, 0.5 cc. (10,000 units) of penicillin subconjunctivally and 1.5 cc. retrobulbarly. Four days later the eye underwent painless shrinkage. The inflammation ceased. The eye is now a good support for a motility prosthesis.

As in many other cases, the penicillin injected intramuscularly was incapable of penetrating into the blood-aqueous barrier in a concentration sufficient for a satisfactory effect. In order to obtain a suitable concentration of penicillin in the aqueous chamber, one should, as shown by the animal experiments of Struble and Bellows, and Sorsby and Ungar, apply 40 to 50 times the usual doses. The fact that rather high doses of penicillin failed to prevent the development of endophthalmitis can thus be explained.

Similar cases occur rather frequently in ophthalmic practice—a foreign body penetrating the eyeball may be removed in good time and yet the infection cannot be combated. Ida Mann reported on 28 patients treated for penetrating injuries. To combat intraocular infection she injected penicillin into the chamber, through a keratome incision by means of a lacrimal cannula; 0.25 cc. of penicillin solution, containing 1,000 to 50,000 units, was given at each treatment. The more diluted solutions had a more favor-

able effect. The sight of two eyes was saved; in 15 eyes vision was lost; 12 enucleations had to be performed.

Case 4. One eye of a man, aged 48 years, was perforated by a copper wire the end of which penetrated into the lens. The protruding end of the wire could be grasped at the center of the cornea with Kalt's forceps. Three days after the injury endophthalmitis set in. Although the exudate filling the lower third of the chamber was repeatedly tapped and massive doses of sulfonamide, together with foreign-protein therapy, were administered, the inflammation did not subside. Then we injected, once a day for three days, 0.2 cc. (4,000 units) of penicillin into the chamber, 0.8 cc. (16,000 units) subconjunctivally, and 1.0 cc. retrobulbarly, directly after the puncture. The 120,000 units given locally caused the inflammation to recede. The wound healed with occlusion of the pupil. Six months later the eye was soft and perception of light was good.

As may be seen, the penicillin therapy given did not preserve the eyeball. Earlier I had a patient (Orvostudomanyi Kozlemenyek, 1944) who was treated, after a similar injury, with large doses of sulfapyridine administered by mouth and intravenously for three days. In one of his eyes the endophthalmitis healed with visual acuity complete. Thus sulfonamide treatment seems to be superior to penicillin therapy in endophthalmitis. The following case speaks in favor of this opinion:

Case 5. A man, aged 67 years, had a prostatectomy. After the operation, septicemia occurred, in the course of which the patient lost the sight of one eye. The endophthalmitis was treated with large doses of sulfonamide administered by mouth and intravenously at the same time. In two days the chemosis and exudation receded. Then we received penicillin and injected intramuscularly daily 100,000 units for five days.

The condition of the eye became rapidly worse, and perception of light ceased after some days. The sclera perforated. (Observed at St. John's Hospital.)

It seemed that penicillin therapy could be made more effective by increasing the concentration of the solution administered locally. The drug should be given intramuscularly and solutions of high concentration should, after tapping of the chamber, be injected into the chamber, subconjunctivally and retrobulbarly. This energetic therapy would probably result in the preservation of the eye and the sight. Until this can be done, the local penicillin therapy should be supported by sulfapyridine given simultaneously by mouth and intravenously in large doses. The following case may demonstrate the efficacy of this combined treatment:

Case 6. On June 10, 1948, a young woman, aged 20 years, a factory worker, was admitted to the eye department. One hour previously while at work, she had looked up and, at that moment, a knitting needle fell upon her left eye, and then fell, by virtue of its weight, to the floor.

Examination showed vision to be: R.E., 5/5; L.E., perception of hand motion. The right eye was intact.

The left eye was closed, watering, with conjunctival and ciliary injection and tenderness on pressure. At the limbus, at about the 7-o'clock position, there was a penetrating wound one mm. in diameter. The anterior chamber was shallow, the eyeball soft, the pupil contracted with a sluggish reaction to light. No red reflex could be obtained from the fundus. Atropine and sulfonamides were prescribed.

On June 11th, chemosis, an infiltrated corneal wound, and exudate at the floor of the chamber could be seen. The pupil was medium in width and partly filled with exudate. Through its outer area some red reflex could be seen. The irritation and tenderness of the eyeball was increased. The penetrating wound was cauterized and the chamber was tapped.

After the evacuation of the exudate 0.2 cc. of penicillin (4,000 units) was injected into the chamber through Anel's cannula, 0.8 cc. subconjunctivally, and 2.0 cc. retrobulbarly. Drops of one-percent adrenalin solution were applied. In addition, sulfapyridine was administered three times a day, two tablets each dose by mouth, 5.0 cc. intravenously, and 10 cc. of milk were given subcutaneously. At eight o'clock that evening the temperature was 38.8°C, the chamber clear, the pupil wide, with unchanged exudate. Again penicillin was given subconjunctivally (20,000 units) and retrobulbarly (20,000 units) together with 5.0 cc. of sulfapyridine intravenously.

On June 12th, the chemosis was gone, the chamber was clear, the pupil wide, the exudate decreased. A red reflex could be seen on examination of the fundus. Vision was 5/20.

The corneal wound was reopened, the aqueous fluid was allowed to flow, then the chamber was irrigated with 0.5 cc. (10,000 units) of penicillin solution. Three drops of one-percent adrenalin solution were given and atropine was instilled repeatedly. Sulfapyridine was prescribed by mouth in the same dose. Twenty-five millions of S. typhi were given intravenously. In the evening the temperature rose to 40°C.

By June 13th, the eyeball was no longer tender;

the chamber was clear, the pupil wide. The exudate was reduced to half the pupil. Vision was 5/12. Five times a day atropine was instilled, and three times a day two tablets of sulfapyridine were given by mouth.

On June 14th, the eyeball was less hyperemic. The depth of the chamber was normal. No exudate could be seen in the area of the pupil. The vitreous was slightly turbid, in its inner half shreds of clotted blood were floating. Vision was 5/10. Atropine drops were continued and a protecting glass was prescribed.

When the patient was discharged on June 21st, vision was 5/5 in both eyes. The left eye was still slightly hyperemic. There was a small scar at the corneal border, at about the 7-o'clock position. Behind the scar there were some vitreous floaters. At the inner lower quadrant of the retina there was a grayish yellow spot about one-fourth disc diameter in size. This was where the knitting needle had stopped when it perforated the globe. Around this site, spots and stripes of blood were to be seen. Otherwise, the fundus was intact. The patient was told to continue the atropine instillation and to wear dark glasses for two weeks.

When demonstrated at the Centennial Medical Week, Section on Ophthalmology, on September 6, 1948, the retinal and vitreous hemorrhages were absorbed. In addition to the corneal and retinal scars there was a small opacity at the site of the vitreous hemorrhage. The eyeball was white, the sight complete.

It may be seen from Case 6, local penicillin therapy and general sulfonamide therapy may be combined most effectively. Of course, general conclusions should not be drawn from a single case, but the result in Case 6 is impressive and permits the hope that similar results may be obtained in similar cases through this procedure.

Summary

Local penicillin therapy in posttraumatic, postoperative, and metastatic endophthalmitis should not be expected to be effective unless the dosage is increased. Injection of penicillin into the anterior chamber and vitreous body, as well as subconjunctival and retrobulbar injection, failed to bring about recovery when used separately. Simultaneous application of these procedures combined with corneal puncture can result in preservation of the eye.

The best results can be obtained if local penicillin therapy is combined with the general administration of sulfonamides. When an endophthalmitis occurring after a penetrating injury was treated with penicillin locally and sulfapyridine by mouth and intravenously simultaneously, rapid and complete recovery followed.

II., Zsigmond-u. 17-19.

References

Axenfeld, T.: Graefe's Arch. f. Ophth., **40**:103, 1894.
Dunnington, J. H., and von Sallmann, L.: Arch. Ophth., **32**:353, 1944.
Leopold, I. H., Wiley, M., and Dennis, R.: Am. J. Ophth., **30**:1345, 1947.
Mann, I.: Brit. J. Ophth., **30**:134, 1946.
Parry, T. G. W., Laszlo, G. C., and Penistan, J. L.: Brit. J. Ophth., **29**:479, 1945.
Roenne, G.: Ophthalmologica, **111**:1, 1946.
von Sallmann, L., Meyer, K., and Di Grandi, J.: Arch. Ophth., **32**:179, 1944.
Sorsby, A.: Brit. J. Ophth., **29**:511, 1945.
Sorsby, A., and Ungar, J.: Brit. M. J., **2**:723, 1946.
Van Heuven, J.: Nederl. tijdschr. v. geneesk., **33**:1006, 1946.
Weizenblatt, S.: Arch. Ophth., **36**:736, 1946.

EFFECT OF AUREOMYCIN IN OCULAR COMPLICATIONS OF LEPROSY*

Reports of treatment

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Reports† of rapid improvement in several forms of conjunctivitis and keratitis following the use of ophthalmic aureomycin‡ solution suggested to us that some benefit might be obtained from the use of this antibiotic in the treatment of some of the common ocular complications seen in leprosy. These short term observations are based upon a treatment experience of three months, during which time reports were collected on 30 patients treated with aureomycin and their progress was compared with that of 20 other patients treated only with the ordinary mercurial and boric-acid eye washes routinely used in this hospital. It is admittedly extraordinarily difficult to evaluate clinical improvement in leprosy but it is believed that the objective findings of improvement supported by the evidence of cultures made from the conjunctival sac suggest that aureomycin was of distinct benefit.

All of the 30 patients in the treated group were hospitalized or colony patients with leprosy of many years' standing. Some were blind and five had had enucleation of a diseased eye, which usually results in these cases, in a chronically infected socket.

Keratitis of all degrees from a micropunctate keratitis to a complete clouding of the cornea with a dense precipitate form was included in the group. All of these patients, however, suffer from a chronic conjunctivitis. In many this assumes the form of an inclusion type of conjunctivitis in which the meibomian glands are plugged with thick tenacious material sometimes causing small cysts or an internal chronic hordeoleum.

A further complication seen in an advanced stage in three patients was a chronic dacryocystitis of many years' standing which had resisted all previous treatment efforts. The control group of 20 patients did not have the variety nor extensive pathologic condition existing in the treated group. None of the patients in the 20 control cases had had an enucleation.

Treatment consisted of an instillation twice daily of aureomycin hydrochloride ophthalmic solution‖ prepared by the addition of 5.0 cc. of distilled water to 25 mg. of aureomycin, 25 mg. of sodium borate and 62.5 mg. of sodium chloride. All treatments were given in the clinic or hospital as it was impossible to supply a solution for self-administration by the patients in various parts of the colony. Further, the solution must be made up and used within two days' time.

It should be added that the three patients with dacryocystitis were subjected to an irrigation of the nasal lacrimal duct by direct catheterization once each week, employing approximately 0.5 cc. of the aureomycin solution for each irrigation. Except for this variation of technique in these cases, all other patients received but one or two drops of the solution in the morning and again four or five hours later in the afternoon clinic.

After the first eight weeks of a scheduled twice-daily treatment such a marked clinical

* From the National Leprosarium, Carville, Louisiana. Approved for publication by the Surgeon General, United States Public Health Service.

† Braley, A. E., and Sanders, M.: Aureomycin in ocular infections. J.A.M.A., 138:426 (Oct.) 1948.

‡ Aureomycin for special investigations in leprosy was supplied by the Lederle Laboratories to Dr. F. A. Johansen, medical officer in charge, and to the staff of the U. S. Marine Hospital, Louisiana.

‖ A supply of aureomycin ophthalmic ointment was distributed to each patient in the series with instructions to use it at night before retiring. The universal response from the entire group was reported as burning and irritation of such degree that not more than one or two applications of the ointment were attempted. This preparation was recalled.

improvement had occurred in the entire group that, for the sake of convenience and conservation of our limited supply of aureomycin, the dosage was reduced to one treatment daily.

Irritation was reported as occurring within the first few minutes in a minority of the patients but was not commented upon by more than five or six. All patients continued the treatment without objecting to this minor inconvenience.

Since this entire group of patients had habitually presented themselves for years in the eye clinic for routine irrigations for the removal of crusts and scales from the lid margins, or for the removal of the purulent discharges which accumulate overnight, the treatment with the aureomycin solution was inadvertently begun before we had obtained a control culture as planned.

The first cultures, then, were made after the group had been treated for a period of

TABLE 1

AUREOMYCIN IN OCULAR LEPROSY

Case	No. of 96 treatments taken	Culture A		Culture B		Culture C	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E.
1	83	–	–	–	–	–	–
2	66	–	–	–	–	–	–
3	70	–	–	–	y	o	o
4	57	–	–	o	o	–	–
5 (x)	50	0	ox	–	–	–	–
6 (x)	76	–	ox	–	–	–	–
7	40	–	–	o	o	–	–
8	83	–1	(1)	o	o	C.	C.
9	64	o	o	(2)	(3)	d	d
10	74	–	–	o	o	–	–
11	86	–	–	–	–	–	–
12 (x)	70	ox	(4)	–	(4)	(5)	–
13 (D.C.)	82	–	–	–	–	–	–
14	76	–	–	–	–	–	–
15	51	o	o	–	–	o	o
16 (x)	74	ox	–	y	–	o	o
17	50	–	–	–	–	–	–
18 (D.C.)	79	–	–	–	–	–	–
19 (x)	77	x	–	o	o	–	–
20	61	–	–	–	–	–	–
21	53	y	y	o	o	–	–
22	18*	–	y	o	o	–	–
23	17†	–	–	o	o	–	–
24	66						
25	64			No cultures taken			
26 (D.C.)	52						
27	54						

Culture A taken March 1st, four to five hours after morning treatment.
Culture B taken March 4th, four to five hours after morning treatment.
Culture C taken March 17th, before morning treatment and 24 hours after previous treatment, schedule reduced to one treatment daily for the previous 14 days.

y. Yeasts—various forms.
C. Grossly contaminated, no reading made.
d. Patient died, no terminal culture made.
(1) Gram-positive, Bacillus subtilis.
(2) Gram-negative, Bacillus proteus.
(3) Gram-negative, Bacillus aerobacter.
(4) Staphylococcus albus.
(5) Short thick Gram-negative bacilli, group not determined.
x. Indicates enucleation of eye.
D.C. Dacryocystitis.
* Began treatment late—maximum available 48.
† Began treatment late—maximum available, 24.
o. Culture not taken.

eight weeks. As may be seen in Table 1, the group followed the treatment schedule remarkably well for in this period there were 96 opportunities for treatment and several patients received more than 80. The 27 patients reported in Table 1 received aureomycin ophthalmic solution with a fair degree of regularity between January 5, 1949, and March 1, 1949. No patient is reported in this table who did not take 40 or more treatments in this period, with the exception of two (cases 22 and 23) who began late in the study, one receiving 18 of 48 possible treatments and the second 17 of 24 possible treatments.

The last four patients listed in Table 1 (cases 24, 25, 26, and 27) took the treatment throughout the period with a high degree of regularity, one of these accepting 86 of the 96 treatments available, but cultures were not taken on any one of these four. All showed marked clinical improvement, however, and they all received more than 50 percent of the scheduled treatments.

In Table 2 we account for the remaining three of the 30 patients treated with aureomycin. These three began treatment in January but presented such an irregular attendance record that no attempt was made to catalogue the variable pattern of their visits, which were, however, less than 10 percent of the treatments offered.

One patient in the group reported in Table 1 died of an intercurrent infection. Although 64 treatments had been administered, there was no apparent improvement in the extreme chronic conjunctivitis which he had had for many years. The organisms reported by the bacteriologist on this patient, Case 9, were a Gram-negative bacillus of the proteus group and a second bacillus of the aerobacter group.

Cultures were made on a total of 50 patients, 30 being treated with aureomycin and 20 controls not treated with aureomycin. Plates were poured with proteose-tryptone agar (difco). The secondary invading organisms in the conjunctiva were Gram-positive Bacillus subtilis in pure culture; Staphylococcus aureus in pure culture; a Gram-negative bacillus of the proteus group; a Gram-negative bacillus of the aerobacter group; and several forms of yeast.

At the end of eight weeks' treatment schedule, the first cultures on the treatment group were made in the afternoon, four to

TABLE 2

PATIENTS RECEIVING LESS THAN 10 PERCENT OF TREATMENTS AT IRREGULAR INTERVALS

Case	No. of 96 treatments taken	Culture A.		Culture B.		Culture C.	
		R.E.	L.E.	R.E.	L.E.	R.E.	L.E.
28	undetermined	–	–	0	o	(4)	(4)
29	undetermined	–	–	–	–	–	–
30	undetermined	0	o	y	–	o	o

TABLE 3

CULTURES ON CONTROL GROUP WITH NO AUREOMYCIN THERAPY

Case	Culture	
	R.E.	L.E.
31	(4)	(4)
32	(5)	(5)
33	–	–
34	–	–
35	–	–
36	–	–
37	–	–
38	(4)	(4)
39	–	–
40	(4)	(4)
41	–	–
42	–	–
43	–	–
44	–	–
45	(5)	(5)
46	y	–
47	(4)	(4)
48	(4)	(4)
49	–	–
50	–	–

five hours after the morning treatment. As can be seen from Table 1—Culture A—all plates were sterile, with the exception of Case 8 which showed Gram-positive Bacillus subtilis and Case 21 and Case 22 which showed yeasts.

Three days later Culture B was taken before the morning treatment and after a lapse of 19 to 20 hours following the afternoon treatment of the previous day. All cultures were sterile with but two exceptions, Case 9 (this patient subsequently died) and Case 12 which showed Staphylococcus albus in pure culture. This patient has an extensive keratitis in this remaining left eye together with a severe chronic conjunctivitis involving the socket of the enucleated right eye. As the various yeast forms observed in four patients of the group were irregularly reported we omit their consideration in this study of secondary organisms. Therefore, it is seen that only three of the 23 patients who followed a satisfactory treatment schedule showed invading secondary organisms in their conjunctival sacs. This improvement was subsequent to a treatment schedule calling for aureomycin instillations twice daily.

The improvement observed clinically and supported by bacteriologic examinations on this group contrasts sharply with the findings in 20 patients, not treated with aureomycin, who received only routine care but from whom cultures were made by the same methods and at the same time. Seven of these 20 patients showed infection with Staphylococcus albus or Gram-negative bacilli, although their ocular complications and leprosy were less extensive and not so advanced as in the treated group.

From a clinical viewpoint, the improvement observed in the 30 cases treated with aureomycin was remarkable. The conjunctiva became firm, free of crusts, and light pink in color in contrast to the edema and beef-redness of chronic conjunctivitis. There was a real and considerable improvement in the appearance of the cornea with a degree of brilliance restored to the surfaces.

On slitlamp examination the areas of superficial punctate keratitis, sometimes seen as small plaques on the surface, had improved. The plaques tended to disappear, leaving only a pitting on a surface otherwise free of damage. There was no alteration in the deeper diffused keratitis along the course of the corneal nerves in the superior temporal quadrants. Improvement was also observed on the surfaces of those corneas which had become nearly completely opaque with a precipitate type of keratitis throughout the substantia propria.

Although no aureomycin was available for simultaneous oral administration in most cases, one patient was treated with rather heroic doses of aureomycin by mouth. He received 2,000 mg. in one 24-hour period. This patient was suffering from an acute leprous iridocyclitis of his left and only remaining eye. Aureomycin ophthalmic solution was instilled locally on a three-hour schedule for 24 hours and two capsules (250 mg. each) of aureomycin were administrated four times in this period. In addition the patient was treated with one-percent pilocarpine* once daily for two successive days.

Within 36 hours, this patient had recovered completely. The entire bulbar conjunctiva was free from congestion, the intense circumcorneal injection had disappeared, and the response of the whole process of leprous iridocyclitis was more than gratifying to both the patient and ourselves. We believe that the internal use of aureomycin contributed to the marked clinical improvement in the course of this condition, a severe ocular complication of leprosy.

* In the iridocyclitis of leprosy, a glaucoma syndrome of moderate degree is associated with this explosive and destructive complication. We have found in the past two years that pilocarpine gives prompt relief from the pain and that its cautious use generally results in improvement within 72 hours. Occasionally, when response to pilocarpine therapy has not followed within this time we have administered streptomycin (0.5 gm.) intramuscularly once daily. Formerly, when treated with atropine and various forms of foreign protein intramuscularly, these patients remained in the hospital for 2, 3, or 4 weeks.

Conclusion

In a group of 30 patients with leprosy and ocular complications resulting from both the leprosy and the secondary invading organisms commonly found in the conjunctival sacs, both clinical and bacteriologic evidence indicated that improvement followed the use of aureomycin ophthalmic solution. It is our impression that many of the disabling and damaging effects, which follow secondary infections in patients having leprosy, can be prevented if the eyes can be kept relatively free from these invaders. In one patient aureomycin by mouth seemed to alter decidedly the course of an attack of leprous iridocyclitis.

Summary

1. Aureomycin ophthalmic solution, even when applied no more than once daily effectively reduces the number of secondary invading organisms found in the conjunctival sacs of leprous patients, as was demonstrated by cultures.

2. Clinical improvement of an unusual degree followed the use of aureomycin in this group of 30 patients with the common extraocular complications seen in leprosy.

3. The experience in one case treated with aureomycin by mouth suggests that further studies of aureomycin in the treatment of leprosy itself should be made, for the clinical course of the iridocyclitis of leprosy was most favorably influenced.

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THE EXPERIMENTAL USE OF CORTISONE IN INFLAMMATORY EYE DISEASE*

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Inflammatory disease of the eye is frequently treated with artificial fever, usually provoked by parenteral foreign protein. In a previous paper,[1] we suggested that the therapeutic benefits are derived from an acceleration of mechanisms normally evoked in many acute stress states. In this respect, the results of many investigators have been such as to ascribe a basic role to the pituitary-adrenal system.[2-4] Indeed, Sayers and Sayers[5] have shown in the experimental animal that both heat and injected killed-typhoid organisms produce changes in the adrenal cortex which are characteristic of the response to stress. Talbot and others[6] and Venning and others[7] have shown that, following a variety of stress states, there is a pronounced increase in the urinary excretion of 11-oxycorticosteroidlike material. A similar increased excretion in human beings has been demonstrated by Forsham and others,[8] Mason and others,[9] and Sprague and others,[10] following the administration of pituitary adrenocorticotropin. It has been postulated by Selye[6] and Albright[11] that the response to stress is achieved to a great extent through an increased elaboration of the adrenal 11-oxycorticosteroids.

In our first report,[1] which covers the experimental use of adrenocorticotropic hormone (ACTH) in the treatment of inflammatory eye disease, results were presented which equalled or exceeded those that are obtained with present-day methods of therapy. It is felt that this was achieved by an adrenal response through stimulation from the injected ACTH which surpassed

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the physiologic response to fever-induced stress. On the premise that the released 11-oxycorticosteroids were the active principles effecting these changes, it seemed logical to determine whether or not this group of steroids administered directly would produce results comparable to those achieved with ACTH.

Other theoretic considerations existed for the trial of 11-oxycorticosteroids in the treatment of ocular disease. It is apparent that ACTH would benefit only those who had adequate adrenal response. Moreover, a few undesirable features may be encountered with ACTH which might be avoided by the use of an 11-oxycorticosteroid. In particular, this would apply to patients with certain types of cardiorenal disease, who might not tolerate the effects of either fever therapy or the prolonged injection of the pituitary hormone.

Recognizing the limitations of our knowledge of corneal permeability, it might be possible for these steroids to act directly upon corneal lesions. Furthermore, minute quantities might be absorbed into the anterior chamber to influence favorably inflammatory lesions involving this segment of the eye. Since one of these 11-oxycorticosteroids, cortisone,* has been made available for experimental studies, it has been used in a series similar to that previously treated with ACTH. To date sufficient observations have been made on seven patients to justify the present report.

Clinical Studies

Case Material

Patients† for this study were drawn from the out-patient clinic of the Division of Ophthalmology of the Henry Ford Hospital. With one exception, Case 6, patients were admitted to the hospital where a complete physical examination and detailed ophthalmologic studies were made. Apart from the eye findings the physical examinations were essentially negative except as follows: Case 1 had a minimal and inactive rheumatoid involvement of the interphalangeal joints of the hands; Case 4 showed generalized arteriosclerosis and mild hypertension; and Case 5 had chronically infected tonsils.

Case 1. A 48-year-old woman had been hospitalized previously with acute plastic iritis. On her last admission, December, 1949, she recovered promptly on ACTH. Two months after her discharge she was readmitted with an acute plastic iritis involving the same eye.

Case 2. A 15-year-old girl had a bilateral congenital luetic keratitis.

Case 3 was that of a 48-year-old man with retinitis centralis and an absolute central scotoma.

Case 4 was that of a 66-year-old woman with acute iritis.

Case 5. A 35-year-old woman had an acute plastic iritis.

Case 6. A 63-year-old man suffered from a severe keratitis and a secondary anterior uveitis. He had been treated previously in this hospital with ACTH.

Case 7 was that of a 53-year-old woman who had a keratitis and secondary anterior uveitis.

Laboratory and Clinical Studies

The five patients admitted to the hospital for parenteral cortisone received the following initial laboratory studies: Complete blood count; direct eosinophil count according to the method described by Forsham and others;[9] a blood Wassermann; and a routine urine examination.

* The 11-dehydro-17-hydroxycorticosterone, cortisone, in the acetate form (Cortone acetate of Merck) was made available through the courtesy of Dr. J. M. Carlisle, Medical Director, Merck Laboratories, Rahway, New Jersey. This preparation is a crystalline suspension of cortisone acetate, 25 mg. per cc., in normal saline with a 1.5 percent benzyl alcohol as a preservative.

† We are indebted to Dr. Harold F. Falls, Ann Arbor, Michigan, Dr. Robert E. Anslow, Detroit, Michigan, Dr. Fleming Barbour, Flint, Michigan, and Dr. John Wetzel, Port Huron, Michigan, for referring four of these patients to us for study.

Prior to, and during, the administration of cortisone, patients received a standard breakfast of determined carbohydrate content, and blood sugars were taken fasting and one hour after breakfast. This served to indicate any changes in carbohydrate tolerance.

As one measure of response, eosinophil counts were taken prior to, four hours, and 24 hours following the administration of the first dose of cortisone. Thereafter they were taken at 24- or 48-hour intervals. As another index, white blood counts and differentials were made at varying intervals.

Body weight, fluid intake and urinary output were recorded daily. Blood pressures were charted twice daily. Other studies not essential to the present report were carried out on some patients.

Ophthalmologic observations were made immediately prior to the first administration of the drug and then at 1-, 2-, 4-, and 8-hour intervals. Thereafter, examinations were made twice daily.

Treatment

Cortisone acetate was administered intramuscularly with initial dosages of 50 mg. every four hours. As the patient responded, either the same dosage was given at increasingly longer intervals or it was reduced to 25 mg. every four hours.

Total dosages of parenteral cortisone acetate ranged from 425 mg. in Case 4 to 2,450 mg. in Case 2.

In Case 2 the patient was started on ACTH, but when she failed in three days to show adequate clinical response she was shifted to parenteral cortisone. When this was discontinued 11 days later, a saline-diluted suspension of the drug was administered topically. The preparation for topical use was made by diluting one volume of the original crystalline suspension with four volumes of isotonic saline. One drop was applied every 30 to 60 minutes during the waking hours.

Local application in Case 1 was begun 17 days after her discharge from the hospital when she again showed signs of a recurrent iritis. Case 6, who was treated as an outpatient, followed the same program of local administration as carried out in the hospital. Case 7 received only topical cortisone both during and after hospitalization.

Except for dilatation with either atropine or homatropine the patients received no definitive therapy during hormonal treatment.

Results

In general, the patients on parenteral cortisone experienced the same sense of well-being as observed in those receiving ACTH. Except in Case 1, who complained of mild depression and some generalized weakness, withdrawal of the drug produced no significant symptoms. To date, no complications have been observed.

The eosinophil count in the five patients treated parenterally fell at least 50 percent by the fourth hour in three, and by the 24th and 48th hour in the remaining two. In the three patients who had frequent eosinophil counts, the reduction in cells appeared to correlate with the initial changes in the ocular lesion.

The therapeutic action of parenteral cortisone was reflected in the rapid subjective and objective improvements which occurred in four of the five patients. The three patients with iritis (Cases 1, 4, and 5) experienced complete relief of pain within the first hour after the onset of treatment. The photophobia in two disappeared within the first hour, and in the third by the end of the 24th hour.

The exudative features of iritis disappeared as rapidly as in similar cases treated with ACTH. Case 1 showed only small clumps of fibrin and these were lysed by the end of the first hour. In the other two cases, the free fibrin was gone from the anterior chamber by the end of 24 hours. In all three cases, the aqueous was completely clear in 72 hours except for an occasional cell.

The luetic keratitis in Case 2 did not respond to three days of ACTH therapy. In

fact, clinically the lesion became worse, and this prompted the change to parenteral cortisone. During the first two days of cortisone the disciform lesions became more dense, but then gradual peripheral clearing began and continued with topical cortisone.

One case of acute recurrent plastic iritis (Case 1) is of special interest. The patient previously had responded well to ACTH and, when retreated with parenteral cortisone, the remission was rapid and complete. Seventeen days after she was discharged from the hospital she again developed signs and symptoms of iritis. This time she was placed on topical cortisone, and when reëxamined at the end of 24 hours she was symptom free and the eye was completely clear.

The patient with retinitis centralis (Case 3) showed an absolute central scotoma to a 1- and 3-mm. white target and vision of 20/137 prior to treatment. Four hours after the initial injection, his visual acuity had improved to 20/86−1. He could now see the 3-mm. target throughout the entire central area, but an absolute scotoma with the 1-mm. target remained. When therapy was discontinued on the seventh day, the visual acuity was 20/20, the tangent-screen examination was normal, and only a small area of depigmentation was visible on funduscopic examination.

In Case 6, the severe keratitis and secondary anterior uveitis recurred on withdrawal of ACTH. One week after the institution of topical cortisone, there were no signs of anterior uveitis and the corneal clearing was equal to that obtained with ACTH.

The second patient with keratitis and anterior uveitis (Case 7) showed marked improvement after 48 hours of topical cortisone. At the end of 17 days of therapy, only 2 or 3 small crenating keratic precipitates and some stromal stippling remained.

Case reports

Case 1

S. S. O., a white woman, aged 48 years, had previously been treated at the Henry Ford Hospital for recurrent attacks of iritis of the right eye. On her last admission in December, 1949, she responded rapidly to ACTH therapy. She was readmitted March 1, 1950, with pain and photophobia, O.D., of about 24 hours' duration.

Apart from the ophthalmic findings, physical examination revealed only minimal enlargement and stiffness of the interphalangeal joints of the hands. There was marked circumcorneal injection with moderate wrinkling of Descemet's membrane, O.D. Slitlamp examination revealed a three-plus flare with many cells and fibrin clumps in the aqueous. There were no keratic precipitates. The iris vessels were dilated and moderate numbers of fresh posterior synechias were present.

Admission laboratory studies were as follows: Hgb., 11.9 gm. percent; R.B.C., 4.1 million; W.B.C., 7,400 with a differential of 57 P.M.N., 40 S.L., and 3 M. Kline exclusion was negative; urine was normal. Fasting blood sugar was 100 mg. percent.

Intramuscular cortisone in dosages of 50 mg. every four hours was started at noon on March 2, 1950. Two hours later, slitlamp examination revealed fewer cells and no clumps of fibrin. Pain and photophobia had disappeared. At the end of 24 hours the number of cells was markedly reduced and only a 1-plus flare remained. The blood eosinophil count in four hours was 92 and thereafter ranged between 5 and 25 per c.mm. No change in the modified carbohydrate tolerance was observed during the three days of treatment.

She continued rapid improvement and by 72 hours the eye was clear except for an occasional cell and mild conjunctival injection. Cortisone was discontinued at the end of the third day after a total of 900 mg. When discharged on the sixth day, the only residual of her iritis was an occasional pigmented cell in the aqueous and one small posterior synechia at the 1-o'clock position.

After an interval of 17 days, during which time the eye remained clear, she returned with mild pain, photophobia, increased conjunctival redness, and a moderate number of fresh cells in the anterior chamber, O.D. One drop of the saline diluted suspension of cortisone was instilled in the eye at hourly intervals. Examination at the end of 24 hours showed no cells in the aqueous. Pain and photophobia had entirely disappeared. Topical cortisone was continued for five days. When last examined on April 3, 1950, the eye was clear.

Case 2

M. L. K., a white girl, aged 15 years, was first examined in our out-patient department on March 4, 1950. This girl had noted loss of vision in her right eye about February 1, 1950. Because of positive serology in both the patient and her mother, she was treated elsewhere with 5,000,000 units of penicillin given over a period of one week. During this antiluetic therapy, visual acuity decreased in her left eye. At no time did she experience pain or photophobia.

The patient was admitted to the hospital on March 5, 1950. With the exception of the eye findings, physical examination revealed no stigmas of

congenital syphilis and was otherwise unremarkable.

Initial laboratory studies gave the following results: Hgb., 13.7 gm. percent; R.B.C., 4.7 million; W.B.C., 8,800 with a differential of 47 P.M.N., 49 S.L., 3 P.M.E., and 1 M.; direct eosinophil count, 264 per c.mm.; urine normal; blood serology: Kline exclusion 4+, Kahn 4+, Eagle 1+, and Kolmer 44,443; spinal fluid protein 17, sugar 63 mg. percent; spinal fluid serology, Kline negative; fasting and one-hour postbreakfast sugars, 97 and 113 mg. percent, respectively.

Visual acuity was light perception, O.D., and 20/32 O.S. Slitlamp examination of the right eye revealed an intense bedewing of the entire corneal epithelium. The deeper layers were opaque with thickening of the entire central area. A faint circular central plaque was observed on the endothelial surface. The anterior chamber and iris could not be visualized. The left eye showed a similar lesion of lesser intensity with a moderate number of cells in the anterior chamber.

Despite the atypical picture, the lesion was considered to be congenital luetic keratitis.

On March 6, 1950, intramuscular ACTH was begun with dosages of 20 mg. every four hours. Within one hour much of the superficial corneal bedewing had disappeared, but this was only transient. After three days of ACTH, totalling 240 mg., the right eye showed no improvement, and on the left a denser disciform type of opacity involved a larger area of cornea. This was evidenced by a decrease in the visual acuity to 20/60. During ACTH, the blood eosinophils dropped to a low of 106.

On March 9th, ACTH was discontinued and intramuscular cortisone was begun, 50 mg. every four hours. Within 24 hours, the eosinophil count fell to 48 and remained at or below this level during the period of parenteral administration. In two days, the corneal bedewing cleared, but the visual acuity, O.S., decreased to 20/200. Thereafter, a slow but definite peripheral clearing of each cornea occurred and visual acuity returned to 20/86, O.S. However, when parenteral cortisone was discontinued on March 20th, after a total of 2,450 mg., there was little change in the central disciform opacities. During this period no adverse general effects were noted, and the modified carbohydrate tolerance remained unchanged.

Topical administration was begun on March 20th, one drop every 30 minutes during the waking period. A more rapid peripheral clearing was evident within the first 24 hours. On April 2nd, the visual acuity had improved to 20/155, O.D., and 20/32, O.S. No cells were now visible in either anterior chamber and the ring deposits on the endothelium had disappeared. Treatment with topical cortisone is being continued. Three weeks after the initial treatment the blood serology remained unchanged.

CASE 3

C. R. L., a white man, aged 48 years, was first seen in the out-patient department on March 10, 1950, with the complaint of blurred vision in his right eye since February 23rd. There was no history of previous eye disease.

On admission the general physical examination was normal. Ophthalmic examination revealed vision to be: O.D., 20/137; O.S., 20/20. There was a small depigmented retinal lesion just nasal to and slightly below the macula, O.D. This was surrounded by an area of hyperemia and edema of one disc diameter. The fundus vessels were normal. On the tangent screen, an absolute central scotoma was charted with the 1- and 3-mm. white targets at a distance of one meter.

Admission laboratory studies were as follows: Hgb. 13.9 gm. percent; R.B.C., 4.1 million; W.B.C., 10,900 with 63 P.M.N., 35 S.L., 1 P.M.E., and 1 M.; urinalysis was normal; Kline exclusion test was negative. The fasting blood sugar was 106 mg. percent, and one hour after a standard breakfast it was 100 mg. percent.

Cortisone in dosages of 50 mg. every four hours was started at noon on March 11, 1950. Tangent-screen examination one hour after the initial injection revealed a relative scotoma with the 3-mm. white target. The absolute scotoma with the 1-mm. white target was still present. Vision was now 20/97. One hour later, and two hours after the initial injection, vision had improved to 20/86—1. There was a smaller absolute central scotoma with the 1-mm. white target but no definite relative scotoma with the 3-mm. target. Twenty-four hours after cortisone treatment was instituted, the vision had improved to 20/52—2 without essential change in the tangent-screen studies. By this time funduscopic examination revealed the original lesion to be smaller with no hyperemia and no significant edema. Improvement was rapid, and by the end of the 5th day, the tangent screen findings were normal. Vision was 20/20. The fundus lesion appeared to be completely resolved except for a small area of depigmentation. Cortisone was discontinued on March 16th after a total of 1,250 mg.

During treatment there was no significant change in the modified glucose tolerance test. The direct eosinophil count was 176 just prior to treatment and fell to 29 within 48 hours after therapy was started. It remained near this level during treatment. A small paracentral scotoma appeared two days after hormonal therapy was discontinued but there was no loss of visual acuity or visible fundus change. The scotoma disappeared the following day.

CASE 4

J. K., a white woman, aged 66 years, was first seen in the out-patient department on March 18, 1950, for a complaint of pain and photophobia in the right eye of three days' duration. There was no history of previous ocular inflammation.

General physical examination on admission revealed a blood pressure of 180/94 mm. Hg and a moderate, generalized arteriosclerosis. Moderate circumcorneal injection was present, O.D.

Slitlamp examination revealed wrinkling of Des-

cemet's membrane, two-plus flare and moderate numbers of cells and occasional puffs of fibrin in the anterior chamber. Early synechias were present.

Initial laboratory studies were as follows: Hgb., 13.1 mg. percent; R.B.C., 4.4 million; W.B.C., 6,400 with a differential of 65 P.M.N., 1 M.N.E., and 34 L.L.; direct eosinophil count, 144 per c.mm.; urinalysis, normal; Kline exclusion test, negative; fasting and postbreakfast sugars, 106 and 146 mg. percent, respectively.

The ophthalmic findings were the same just prior to the first injection of cortisone on March 19th, except that the synechias had been broken. One hour after the first 50 mg. of cortisone, pain and photophobia disappeared. No fibrin puffs or flare were visible, and there was a marked reduction in the number of cells. After the second injection, cortisone was reduced to 25 mg. every four hours. After 48 hours, only an occasional cell remained in the anterior chamber and cortisone was discontinued with a total of 425 mg. Blood eosinophils at that time were 32 per c.mm. On reëxamination on March 29th the eye was perfectly clear.

Case 5

B. M. W., a white woman, aged 35 years, was seen in the out-patient department on March 24, 1950. Her presenting symptoms were pain, photophobia, and redness of the right eye of one-week duration. There was no history of previous ocular inflammation.

With the exception of the eye lesion, the only abnormality found on admission examination was chronically infected tonsillar tags. The right eye showed marked circumcorneal injection. Slitlamp examination revealed considerable wrinkling of Descemet's membrane. There were many fine cells in the anterior chamber and a three-plus flare. Two large masses of fibrin were present at the 3 to 6- and 7 to 9-o'clock positions.

Initial laboratory studies were as follows: Hgb., 14.7 mg. percent; R.B.C., 4.8 million; W.B.C., 10,800 with 68 P.M.N., 1 P.M.E., and 31 L.L.; direct eosinophil count, 77; urine, normal; Kline exclusion, negative; fasting and one-hour postbreakfast sugar 85 and 97 mg. percent respectively.

Cortisone in initial doses of 50 mg. every four hours was started at noon on March 25, 1950. One hour later she was free of pain and complained only of mild photophobia. The blood eosinophils at this time were 25 per c.mm., and remained below this level throughout the period of treatment.

Examination at the end of the second hour revealed less circumcorneal injection and a definite decrease in the cells and flare. The two masses of fibrin were noticeably smaller. At the end of 24 hours, the fibrin was completely absorbed from the anterior chamber. Photophobia was absent. The flare was much less and disappeared by the end of 36 hours. At this time Descemet's membrane had cleared and the only residuals of the iritis were a few cells in the anterior chamber and slight circumcorneal injection.

By March 30th, only a rare cell could be visualized in the anterior chamber and the eye was otherwise clear. Cortisone was discontinued on March 30th after a total dosage of 1,350 mg. A tonsillectomy for the removal of the only known focus of infection was performed on April 3rd. When last examined, April 4th, no signs or symptoms of iritis were present.

Case 6

G. R., a white man, aged 62 years, had previously been hospitalized at the Henry Ford Hospital for a severe keratitis and secondary anterior uveitis, O.D., of three months' duration. Examination at the time revealed a nearly opaque cornea with a bullous keratitis and early pannus formation. Even after glycerin it was impossible to determine the exact amount of exudate in the anterior chamber, but large mutton-fat keratic precipitates were present in the central area. Tension, O.D., was 40 mm. Hg (Schiøtz). There was moderate circumcorneal injection.

A total of 695 mg. of ACTH was given from January 26 to February 9, 1950. With this therapy the corneal edema rapidly cleared and tension fell to normal. The exudate then visible in the anterior chamber disappeared completely and the corneal stroma became much less opaque. A dense secondary cataract became visible and, accordingly, visual acuity could not be used as an index for improvement.

The patient was discharged from the hospital on February 19th. The examination on February 25th revealed regression to the pretreatment level. On March 18th, there was no essential change. Tension, O.D., was 35 mm. Hg (Schiøtz). Topical cortisone was then started, using one drop every hour during the waking period. One week later there was marked improvement. Tension was 30 mm. Hg. There was much less circumcorneal injection and the cornea was definitely clearer. There were few keratic precipitates and cells in the anterior chamber. When last examined, March 31st, the cornea had reached the maximum clearing that occurred with ACTH. There was practically no circumcorneal injection and no cells in the anterior chamber. The few remaining keratic precipitates were crenating. Tension was now 23 mm. Hg. Treatment with topical cortisone is being continued.

Case 7

G. N. G., a white woman, aged 53 years, developed a localized area of corneal edema, O.S., prior to examination on March 8, 1950. This progressed to involve three fourths of the cornea. An anterior uveitis and a secondary glaucoma followed despite heavy typhoid-H antigen therapy, penicillin, salicylates, and atropine administered elsewhere.

On admission to the hospital, March 8th, general physical examination was within normal limits. No foci of infection were found and tuberculin and brucella skin tests were negative. Visual acuity,

O.S., was reduced to 20/137—1. Slitlamp examination revealed bedewing over the lateral three fourths of the cornea, with the stroma showing increased thickness and cloudiness. There were several large plaquelike precipitates and numerous small keratic precipitates over the posterior cornea, and the entire endothelial surface was covered with fine linear deposits of fibrin. A moderate number of cells were present in the anterior chamber. Intraocular pressure, O.S., was 27 mm. Hg (Schiøtz).

Initial laboratory studies were as follows: Hgb. 12.6 mg. percent; R.B.C., 3.9 million; W.B.C., 6,500 with a differential of 45 P.M.N., 1 P.M.B., 50 S.L., 4 M.; Kline exclusion, negative; urinalysis, normal; fasting blood sugar, 97 mg. percent.

Topical cortisone was given, two drops every hour. After 48 hours, a marked improvement occurred with definite diminution of the edema and clearing of the stroma. There were fewer cells in the aqueous. On the ninth day, the edema had disappeared and the cornea was definitely clearer. No fibrin was present on the endothelium and the keratic precipitates were markedly thinned and crenated. Only an occasional cell remained in the anterior chamber. Tension was 18 mm. Hg (Schiøtz). Topical application was reduced to two drops every three hours.

Eight days later the aqueous was clear and only a fine, diffused stippling in the stroma of the involved area was observed. The keratic precipitates had practically disappeared. Tension was 15 mm. Hg, and visual acuity had improved to 20/86. Local cortisone therapy is being continued.

Discussion

The present study has demonstrated that parenteral 11-deyhdro-17-hydroxycorticosterone acetate (cortisone acetate) is effective in resolving certain inflammatory diseases of the eye. Despite the limited number of cases that have been studied, it seems definite that cortisone causes a more rapid resolution of these lesions than the presently employed foreign-protein therapy. It should be pointed out that the therapeutic benefits derived from cortisone do not justify omission of the time-honored search for the possible etiologic factors in ocular inflammatory disease. In the light of present concepts,[4] however, it may be postulated that certain inflammatory eye diseases are a direct reflection of altered adrenal physiology. This might apply not only to the individual under prolonged stress, but also to the individual with a relative adrenal-cortical hypofunction. If this postulate proves true, cortisone would appear to have a more specific role in therapy.

Another possible advantage of this agent is the fact that control of certain inflammatory lesions can be effected in a few hours, as contrasted to the time that is frequently required with current methods of therapy. In addition, patients receiving cortisone in this study did not demonstrate any side effects. With the exception of Case 2, treatment was relatively brief, and this fact may have obviated in part the possible undesirable complications.

At the present time cortisone appears to be as effective as ACTH in the treatment of certain inflammatory eye diseases. Further experience may delineate more selective application for each. However, patients may be encountered in whom the use of either fever therapy or ACTH may be limited. For example, this might apply to patients with hypertension, congestive failure, or advanced, degenerative renal disease. In addition, there may be patients with insufficient adrenal reserve who would not respond adequately to fever or to ACTH. The direct action of cortisone obviates this. The favorable response of acute inflammatory lesions to cortisone reported here in no way suggests that future relapses will be prevented.

The results of topical application in the case of luetic keratitis cannot be properly evaluated. It is possible that the lesion might have cleared had ACTH been continued longer. Furthermore, the improvement which followed topical cortisone may have represented a delayed beneficial response to parenteral cortisone.

It appears significant to us that the other three patients treated with topical cortisone alone showed a definite and favorable response. This suggests that cortisone may act directly at the local tissue level and also penetrate the cornea in amounts sufficient to alter favorably inflammations of the anterior segment of the eye. The implications of this are apparent but no conclusions can be drawn until further investigation is completed.

The observations reported here lend support to the concept that cortisone, and possibly other steroids with similar physiologic activity, are of importance in the response of the organisms to inflammatory processes. This limited series does not allow any broad conclusions as to the efficacy of cortisone in other eye diseases. Its broader application is currently under investigation.

Summary

11-dehydro-17-hydroxycorticosterone acetate (cortisone acetate) has been used in the experimental treatment of seven patients with inflammatory eye disease. Both parenteral and topical modes of administration were employed.

Four patients received parenteral cortisone alone and all responded favorably. One of these later relapsed and was successfully retreated with topical cortisone.

The patient with congenital luetic keratitis, who initially received ACTH and then parenteral cortisone continued improving when topical cortisone was employed, but the role of the latter cannot be evaluated.

The two cases of keratitis with anterior uveitis showed definite improvement with topical cortisone alone.

The results of treatment with cortisone have been evaluated in the light of our previous experience with ACTH and fever therapy, and its possible merits discussed. Further investigation is necessary before any final conclusion can be drawn.

Henry Ford Hospital (2).

References

1. Olson, J. A., Steffensen, E. H., Margulis, R. R., Smith, R. W., and Whitney, E. L.: The effect of ACTH on certain inflammatory diseases of the eye: A preliminary report. J.A.M.A., **142**:1276-1279, 1950.

2. Sayers, G., Sayers, M. A., Liang, T. Y., and Long, C. N. H.: The cholesterol-and ascorbic acid content of the adrenal, liver, brain and plasma following hemorrhage. Endocrinology, **37**:96-110, 1945.

3. Pincus, G.: Studies of the role of the adrenal cortex in the stress of human subjects. Recent Progress in Hormone Research, **1**:123, 1947.

4. Selye, H.: The general adaptation syndrome and the diseases of adaptation. J. Clin. Endocrinol., **6**:117-230, 1946.

5. Sayers, G., and Sayers, M. A.: The pituitary-adrenal system. Ann. New York Acad. Sc., **50**: 522-539, 1949.

6. Talbot, N. B., Albright, F., Saltzman, A. N. Zygmuntowicz, A., and Wixom, R.: The excretion of 11-oxycorticosteroid-like substances by normal and abnormal subjects. J. Clin. Endocrinol., **7**:331-350, 1947.

7. Venning, E. H., Hoffman, M. M., and Browne, J. S. L.: The extraction of cortin-like substances from human post-operative urine. Endocrinology, **35**:49-62, 1944.

8. Forsham, P. H., Thorn, G. W., Prunty, F. T. G., and Hills, A. G.: Studies with pituitary adrenocorticotropin. J. Clin. Endocrinol., **8**:15-66, 1948.

9. Mason, H. L., Power, M. H., Rynearson, E. H., Ciaramelli, L. C., Li, C. H. and Evans, H. M.: Results of administration of anterior pituitary adrenocorticotropic hormone to a normal human subject. J. Clin. Endocrinol., **8**:1-14, 1948.

10. Sprague, R. G., Power, M. H., Mason, H. L., Albert, A., Mathieson, D. R., Hench, P. S., Kendall, E. C., Slocumb, C. H., and Polley, H. F.: Observations on the physiologic effects of cortisone and ACTH in man. Arch. Int. Med., **85**:199-258, 1950.

11. Albright, F.: Cushing's syndrome: Its pathological physiology, its relationship to the adrenogenital syndrome, and its connection with the problem of the reaction of the body to injurious agents ("Alarm reaction" of Selye). Harvey Lectures, 1942-1943, Baltimore, Williams & Wilkins, 1943.

TRANSPLANTATION OF THE SUPERIOR AND INFERIOR RECTUS MUSCLES FOR PARALYSIS OF THE LATERAL RECTUS*

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It has long been established that complete and prolonged paralysis of the lateral rectus is amenable only to surgical correction. Since Hummelsheim[1] first suggested transplantation of portions of the vertical rectus muscles to enhance the action of a paralyzed lateral rectus, his technique and various modifications have been employed with results which have varied markedly. Transplantation of the extraocular muscles has not been too generally practiced by ophthalmologists. This fact may possibly be attributed to some disappointing results obtained or to the technical difficulties encountered.

Because of the comparatively small number of cases published in the literature to date, 62 in all, and conflicting reports concerning results, a description of the technique employed and results obtained in seven cases are presented.

A RÉSUMÉ OF THE LITERATURE

The literature prior to 1944 covering this subject has been well reviewed and discussed by Langdon and his associates[2] in their paper on the operative treatment of paralysis of the external rectus muscle. Good postoperative results were attained in two cases of traumatic paralysis of the lateral rectus following transplantation of portions of the vertical recti with retroplacement of the medial rectus and advancement of the lateral rectus.

Since 1944, Reinhardt[3] has reported excellent results in six transplantations, using the O'Connor cinch operation for the advancement of the lateral rectus. He advocated prompt surgical intervention before irreversible changes (contractures) occur in the opposing medial rectus. Tenotomy or retroplacement of the internus is indicated if fibrosis has taken place.

In a case of spina bifida with bilateral abducens paralysis, Mangus[4] transplanted the vertical rectus muscles in one eye first and then in the other, each time employing a 5.0-mm. resection of the lateral rectus. Although the cosmetic result was good, the patient obtained no abduction. Gallo and Novick,[5] employing the original technique of Hummelsheim, described one case in which 60 degrees of abduction were obtained postoperatively. Walker,[6] using the Lancaster modification in which the medial rectus is receded in addition to the transplantation, reported two cases with repeated synotophore findings. Both patients had excellent abduction of the affected eye by the 28th postoperative day.

Lutman,[7] employing a technique similar to ours, obtained excellent results in two cases.

The technique of transplantation for muscle paralyses described herein was first published by one of us (C. B.[8] in 1945) in a case of paralysis of the inferior rectus, requiring transplantation of the lateral rectus to the inferior rectus insertion. The first operation on the lateral rectus muscles (Case 7) was performed by one of us (C. B.) in 1941.

TECHNIQUE OF TRANSPLANTATION

Definition. This operation consists of transplantation of the lateral halves and displacement of the nasal half of the superior and inferior rectus muscles temporally, usually combined with resection of the lateral rectus and retroplacement of the medial rectus. Tenon's capsule is transplanted with the muscle.

Instruments. These include: eyelid speculum, Graefe knife, Stevens scissors, blunt straight scissors, fixation forceps, mouse-

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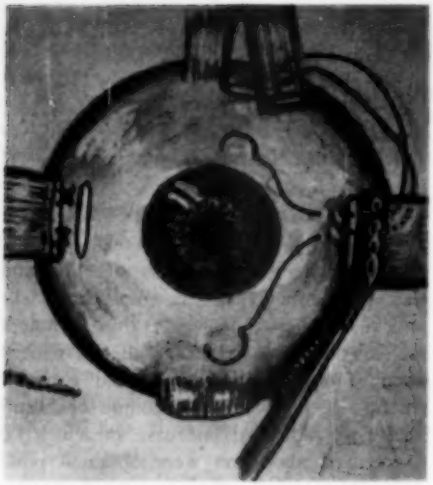


Fig. 1 (Berens and Girard). Technique of transplantation (schematic representation). For clarity Tenon's capsule is not shown. The medial rectus has been retroplaced. The lateral rectus has been resected and is held with muscle forceps. A 10-mm. strip of superior rectus has been separated from the remainder of the muscle. A double-armed 5-0 nylon suture is introduced into the lateral rectus and passed through its free end. The suture is then passed through the lateral rectus stump.

tooth forceps, strabismus scissors, scalpel, millimeter rule, calipers, and muscle forceps (Berens*).

Sutures. The suggested sutures are: blue and white 5-0 nylon and 5-0 plain catgut.

Technique

First stage: Retroplacement of the medial rectus

a. The medial rectus is exposed by means of a conjunctival incision and separated from its insertion.

b. Retroplacement* may be performed using two double-armed 5-0 white nylon sutures (D & D #P417): (1) If the relative or absolute near point is normal or close, a 3.5-mm. retroplacement is usually safe; (2) if the near point is remote and fusion is poor from any cause, it may be advisable to perform retroplacement later; (3) if the esotropia is much greater at distance than at near, and the near point is remote, retroplacement of the medial rectus may not be desirable.

c. The conjunctival wound is closed with a continuous 5-0 plain catgut suture.

Second stage: Resection of the lateral rectus

a. The lateral rectus is exposed by means of a conjunctival incision and the desired amount of resection is performed. The amount of resection performed is determined by the degree of the deviation and by the state of the muscle at the time of operation. In most cases a 7.0-mm. resection is sufficient.

b. The freed muscle is held to one side by a muscle clamp.

Third stage: Transplanting the lateral halves of the superior and inferior rectus muscles with Tenon's capsule to the lateral rectus insertion

a. The insertion of the superior rectus is exposed. The lateral half of the muscle with Tenon's capsule is grasped with muscle forceps and freed from the insertion with Stevens scissors.

b. A strip, approximately 10 mm. in length, of the lateral half of the muscle belly with overlying Tenon's capsule is separated from the remainder of the muscle and a double-armed 5-0 white nylon suture is introduced into the free end.

c. This suture is now passed through the lateral rectus from the scleral surface and then through the jaws of the muscle clamp (fig. 1).

d. The same procedure is performed on the inferior rectus.

e. The four needles are passed through the lateral rectus insertion and are tied.

Fourth stage: Transplanting the medial halves of the superior and inferior rectus muscles temporally

a. The medial half of the superior rectus

* Made by E. B. Meyrowitz & Co.

with Tenon's capsule is detached and sutured to the temporal portion of its insertion, using a 5-0 double-armed blue nylon suture.

b. The medial half of the inferior rectus is treated in a similar manner (fig. 2).

c. The conjunctival wound is closed with a running 5-0 plain catgut suture with a central lock stitch.

Postoperative treatment includes: (a) A light binocular pressure dressing; (b) after 24 hours a Ring's mask is worn with a 1.0-cm. hole before each eye; (c) abducting exercises and fusion training when reaction subsides.

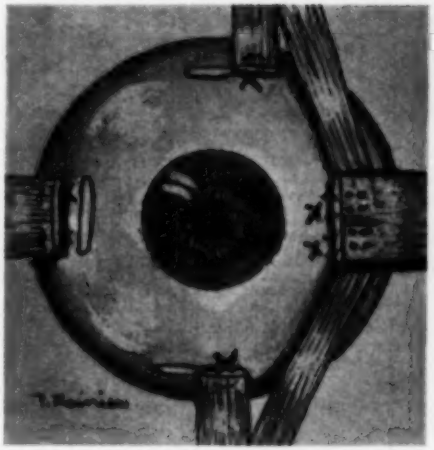


Fig. 2 (Berens and Girard). Technique of transplantation (schematic representation). Tenon's capsule is not shown. Operation has been completed. The medial halves of the vertical rectus muscles now occupy the lateral portions of their insertions.

Case reports

The following cases are described in detail and are tabulated in Table 1.

Case 1.

P. W., a boy, aged eight years, was first examined on December 18, 1946. The patient's mother said that he had been unable to turn his right eye outward since birth. The statement that his father had a convergent squint was the only significant finding in the past or family history.

Examination revealed the following: vision in each eye, uncorrected, 20/20 minus. A weak plus sphere and cylinder improved his vision to 20/20 in each eye. Accommodation was 300-mm. print at 50 mm. for the right eye and 300-mm. print at 60 mm. for the left eye. The cover test with prisms revealed esophoria of 4$^{\Delta}$ at 6.0 M. and 6$^{\Delta}$ at 25 cm. There was, at times, homonymous diplopia at 6.0 M. and a 4$^{\Delta}$ prism base out permitted fusion. With the latter he was able to fuse the Berens three character test. The cover test with prisms in the main diagnostic positions of gaze revealed an esotropia to the right of 30$^{\Delta}$ and above and right of 40$^{\Delta}$.

Study of motility revealed slight weakness of the left lateral rectus, marked underaction of the right lateral rectus, and marked overaction of the left medial rectus. Diplopia fields (fig. 3a) revealed homonymous diplopia to the right and fusion in most of the left field of binocular fixation. Fields of monocular fixation (fig. 3b) taken with a 1.2-mm. letter on the perimeter revealed marked underaction of the right lateral rectus. The right eye could be abducted only 10 degrees. The actions of other muscles of the right eye were normal. The left eye revealed no motor disability. A diagnosis was made of paralysis of the right lateral rectus.

Operation. On May 28, 1947, under general anesthesia, the right lateral rectus was resected 6.0 mm., and the superior and inferior rectus muscles were transplanted. The medial rectus was not receded because the deviation at 25 cm. was minimal and no secondary contracture was present. Postoperative recovery was uneventful.

Two weeks later the patient was able to abduct the right eye 30 degrees when examined on the perimeter. The cover test revealed orthophoria for distance and near. However, the Maddox-rod test revealed esophoria of 4$^{\Delta}$ at 6.0 M. and 25 cm. Abducting exercises and fusion training were prescribed.

On December 22, 1947, examination revealed the following: With the cover test, there was orthophoria for distance and near. The Maddox-rod test elicited an esophoria of 4$^{\Delta}$ at 6.0 M. and 25 cm. Amplitude of vergence was divergence 4$^{\Delta}$ and convergence 12$^{\Delta}$ at 6.0 M., divergence 4$^{\Delta}$ and convergence 20$^{\Delta}$ at 25 cm. The boy was able to abduct his right eye to the lateral canthus (40 degrees on the perimeter). On the orthoptoscope, he showed an esophoria of 5$^{\Delta}$ with an amplitude of 7$^{\Delta}$ base in and 25$^{\Delta}$ base out. Third-grade fusion was present. The diplopia field showed marked improvement (fig. 4a) when compared with the preoperative field, for diplopia was present only in the extreme right field. Fields of monocular fixation (fig. 4b) showed improvement to 50 degrees to the right.

Case 2.

J. G., a girl, aged 19 months, was first examined on November 8, 1945. The patient's pediatrician had noted a convergent squint soon after birth. The family and past history revealed that the

TABLE 1

PREOPERATIVE AND POSTOPERATIVE FINDINGS IN SEVEN CASES OF TRANSPLANTATION OF THE VERTICAL RECTUS MUSCLES

Patient (Age-Sex)	Preoperative Deviation	Paralyzed Muscle	Preoperative Abduction Power	Fusion	Surgery	Postoperative Deviation	Postoperative Abduction Power	Fusion	Remarks
(1) P.W. 8 yr. M.	E 4, E' 6 Cover test with prisms	R.L.R.	Beyond midline 10°	3 character test (Berens) at 6.0 M. Worth dots at 25 cm.	R.L.R. resected 6 mm. Vertical recti transplanted.	0° Cover test E 4 E'4 Maddox rod	40° perimeter	Orthoptoscope 3rd grade with amplitude 7 B.I. to 25 B.O.	Still has slight retraction syndrome
(2) J.G. 19 mo. F.	E^1 48° LH^1 16° (Hirschberg test)	L.L.R.	0°	Unable to measure because of age	L.M.R. receded 2 mm. L.L.R. resected 6 mm. Vertical recti transplanted.	E^1 15$^\Delta$ Cover test at 6 M.	To lateral canthus	Orthoptoscope 2nd grade	Recently seen and abducts left eye to lateral canthus
(3) D.P. 19 mo. M.	E^1 48° LH^1 6° (Hirschberg test)	L.L.R. R.S.R.	0°	Unable to measure because of age	L.M.R. retroplaced 2 mm. L.L.R. resected 6 mm. Vertical recti transplanted.	E^1 20° E^V 16° (Hirschberg test)	To lateral canthus	Orthoptoscope 2nd grade at objective angle	Fixed with O.D., occlusion of O.S. advised
(4) S.W. 1 yr. M.	E^1 60° (L.E.) E^1 50° (R.E.) (Perimeter)	R.L.R.	0°	Unable to measure because of age	R.L.R. resected 10 mm. R.M.R. retroplaced 2.5 mm. Vertical recti transplanted.	LH^1 10$^\Delta$ Cover test with correction	1. To lateral canthus. 2. 50° perimeter	Orthoptoscope 2nd grade	Almost complete aplasia of right lateral rectus
(5) M.V. 3 yr. F.	E^1 70$^\Delta$ Cover test at 6.0 M.	R.L.R. L.L.R.	0°	Unable to measure because of age	R.L.R. & L.L.R. resected 7 mm. Transplantation vertical recti. Retroplacement R.M.R. & L.M.R. 4 mm.	E-trace X' 6 Cover Test	R. 40° L. 35° Perimeter	Orthoptoscope 2nd grade E 5. Fuses 3 Character test 6.0 M. and 25 cm.	Both medial recti extremely fibrotic
(6) B.D. 19 mo. F.	E^1 36° (Hirschberg test)	L.L.R.	0°	Unable to measure because of age	L.M.R. retroplaced 2.5 mm. L.L.R. resected 8 mm. Vertical recti transplanted.	E^1 16° (Hirschberg test)	To lateral canthus	Too young to measure	Left medial rectus bound down by adhesions to sclera. Insertions of vertical recti (L.E.) measured 5 mm. in diameter
(7) M.L. 39 yr. M.	E^1 40$^\Delta$ E^V 40 Cover test	L.I.R.	0°	Orthoptoscope 2nd grade with 30–40$^\Delta$ base out. Unable to fuse 3 character test	L.M.R. retroplaced 3.5 mm. L.L.R. resected 8 mm. Vertical recti transplanted.	E 10$^\Delta$ LH 1.5 Cover test	To lateral canthus	Orthoptoscope 3rd grade. Fuses 3 character & Worth 4-dot tests	Was able to maintain binocular single vision 10° to left of midline

Key to abbreviations: E, esophoria; E^1, esotropia; LH, left hyperphoira; LH^1, left hypertropia; $^\Delta$, prism diopter and °, degree.

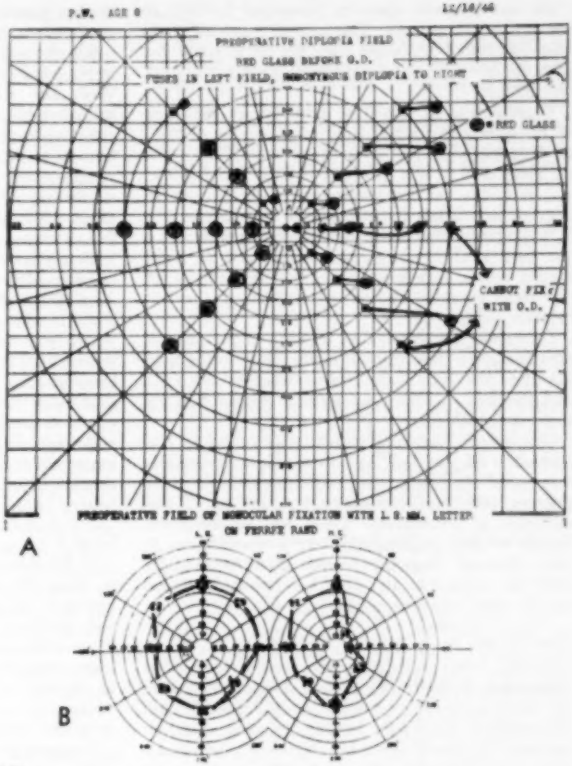


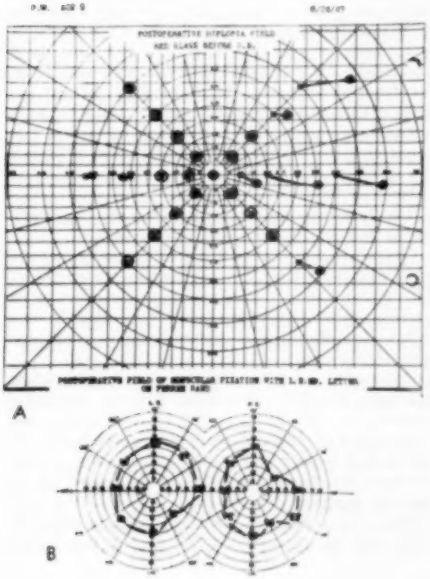
Fig. 3 (Berens and Girard). (A) Preoperative diplopia fields, Case 1. (B) Preoperative fields of monocular fixation, Case 1.

father had a squint and that the patient had been delivered with low forceps.

Examination was limited because of the child's age. With the retinoscope reversal was observable at +1.75D. sph. in each eye at 66 cm. Ophthalmoscopic examination revealed no pathological condition. The Hirschberg test revealed an esotropia of 48 degrees and left hypertropia of 16 degrees for distance.

The patient was observed again on January 26, 1946, and the same findings were obtained. At this time she was unable to abduct her left eye beyond the midline. A diagnosis was made of complete paralysis of the left lateral rectus with spasm of the left inferior oblique.

Operation. On April 10, 1946, the patient was operated upon under general anesthesia. The left medial rectus was retroplaced 2.0 mm., the left lateral rectus was resected 6.0 mm., and the superior and inferior rectus muscles were transplanted.



One month later she showed an excellent cosmetic result, with abduction to the lateral canthus with ease. On the orthoptoscope she showed second-grade fusion. With the cover test there was an esotropia of 15Δ at six meters.

CASE 3

D. P., a boy, was first seen on January 28, 1946, at the age of 11 months. The child's mother had noticed a convergent squint since birth. Past history revealed that the father had a divergent squint.

Examination. Under cycloplegia a +0.25D. sph. was found by retinoscopy in each eye. He was unable to abduct the left eye beyond the midline. The mother of the patient was given atropine solution (0.25 percent) to instill in the child's right eye, and was instructed to attempt to make the child abduct the left eye.

Fig. 4 (Berens and Girard). (A) Postoperative diplopia fields, Case 1. (B) Postoperative fields of monocular fixation, Case 1.

He was observed again on November 1, 1946, at the age of 19 months. The mother reported that, when occluding the right eye, the child could fix with the left eye but was unable to abduct it beyond the midline.

Examination at this time revealed an esotropia of 48 degrees and a left hypertropia of six degrees at distance with the Hirschberg test. There was no abduction of his left eye beyond the midline. At near, the patient showed an esotropia of 48 degrees with a left hypertropia of 16 degrees.

A diagnosis was made of complete paralysis of the left lateral rectus, overaction of the right medial rectus, left hypertropia due to paralysis of the right superior rectus, and spasm of the left inferior oblique.

Operation. On November 2, 1946, under general anesthesia the left medial rectus was retroplaced 2.0 mm., the left lateral rectus resected 6.0 mm., and the left superior and inferior rectus muscles were transplanted.

One month later the patient was observed and abduction of the left eye to the lateral canthus was noted. At 6.0 M. there was an esotropia of 20 degrees with the Hirschberg test and at 25 cm. esotropia of 16 degrees. There was second-grade fusion at objective angle on the orthoptoscope. It was observed that the patient fixed continually with the right eye and for this reason occlusion of the right eye was advised.

CASE 4

S. W., a boy, aged one year, was first seen on September 27, 1941. The mother had observed that the child was unable to move the right eye beyond the midline. The past history revealed that the mother had been in labor 14 hours when the patient was born and was delivered with low forceps. Mental and physical development were normal.

Examination under cycloplegia revealed: Correction, +1.25D. sph. ⌒ +0.50D. cyl. ax. 75° in the right eye; +2.0D. sph. ⌒ +0.50D. cyl. ax. 100° in the left eye. Using a hand perimeter and with the left eye fixing, esotropia of 60 degrees was noted, and with the right eye fixing an esotropia of 50 degrees. Screening in the cardinal positions of gaze revealed esotropia increasing to the right. The patient was unable to abduct the right eye beyond the midline. Ophthalmoscopic examination revealed no pathologic condition of the fundus.

This patient was also seen by a neurologist who made the following diagnosis: right lateral rectus palsy with nervous-system defect, possible birth injury. The final diagnosis before the operation was complete paralysis of the right lateral rectus.

Operation. On December 11, 1945, under general anesthesia the right medial rectus was retroplaced 2.5 mm., the right lateral rectus was resected 10 mm., and the right superior and inferior rectus muscles were transplanted. It was noted during the operation that there was almost complete aplasia of the right lateral rectus. Two weeks after the operation the child was able to abduct his right eye to the lateral canthus. The cosmetic result was good. He was placed on abducting exercises.

Six months later the cover test revealed esotropia of 20Δ and a trace of a left hypertropia. With his correction, screening showed an esotropia of 10Δ. In September, 1946, the patient was again observed and an esotropia noticed. At this time there was some underaction of the right lateral rectus, overaction of the right inferior oblique, overaction of the right superior oblique, and a slight nystagmoid movement present on looking to the extreme left.

On October 8, 1946, the patient had no esotropia for distance but a left hypertropia of 14Δ. On April 26, 1947, the patient's vision without correction was 20/50 in each eye as determined with the "E" chart. There was no esotropia present but a left hypertropia of 10Δ was noted. He was able to abduct his right eye to the lateral canthus. Fields of monocular fixation showed abduction to the right of 50 degrees but limitation of elevation of the right eye. With the orthoptoscope there was an esotropia of 5Δ and a left hypertropia of 5Δ. He seemed to obtain second-grade fusion at his objective angle.

CASE 5

M. V., a girl, aged three years, was first examined on June 30, 1944. Her mother gave the following history: The patient was born with a meningocele and had been operated upon at 14 weeks of age. Since birth both eyes had turned inward, the left more than the right. Following an encephalogram at the age of two years, the patient developed meningitis resulting in complete recovery under penicillin therapy.

Examination revealed the following: Cycloplegic acceptance: R.E., +1.5D.; L.E., +1.25D. Esotropia of 70Δ was demonstrated at 6.0 M. with the cover test. With cover and uncover test she fixed alternately, but preferred the right eye. At 25 cm. she favored her right eye, fixed with the left eye when a light was placed to her right, and fixed with her right eye when a light was placed to the left. She was able to see 300-mm. print at 100 mm. with each eye ("E" test). There was no lateral rotation of either eye beyond the midline.

The diagnosis was a true paralysis of both lateral rectus muscles with a resultant esotropia.

Operation. On January 23, 1945, under general anesthesia, both lateral rectus muscles were resected 7.0 mm. and then the superior and inferior rectus muscles were transplanted. At this time, it was noted that the medial rectus muscles were extremely fibrotic.

One month later the Hirschberg test revealed an esotropia of 20Δ. Screening without correction showed, at 6.0 M., esotropia of 20Δ and a left hypertropia of 14Δ and, at 25 cm., esotropia of 20Δ and a left hypertropia of 20Δ. There was a good cosmetic result and the patient was placed on abducting exercises.

The child was again observed on September 27, 1945, and an esotropia of 30Δ with a left hyper-

tropia of 9Δ was noted with the screen test; at near there was esotropia of 30Δ and left hypertropia of 9Δ. The patient was able to abduct the right eye five degrees and the left eye 20 degrees. Abducting exercises were continued.

On January 13, 1947, the mother stated that in the interim between the present and the past visit, the patient had developed German measles followed by meningitis. She was again placed on penicillin and made a rapid recovery. At this time her vision was: R.E., 20/40; L.E., 20/30, on the "E" chart. Esotropia of 30Δ at 6.0 M. and 25 cm. was revealed by the screen test. Motility examination revealed fair action of the inferior rectus and superior oblique of each eye. There was marked limitation of action of both lateral rectus muscles.

On May 14, 1947, both medial rectus muscles were retroplaced 4.0 mm. The patient was observed one month later and her vision was 20/40 in each eye on the "E" chart. The cover test revealed esotropia 6Δ and a trace of right hypertropia. She was able to abduct her right eye 25 degrees and her left eye 20 degrees. With the orthoptoscope, without correction, she had an esotropia of 15Δ, and, with correction, an esotropia of 8Δ.

On March 5, 1949, after periodic orthoptic training, examination revealed the following: vision, with correction, was 20/30 in each eye. The screen test showed, at 6.0 M., a trace of esophoria; at 25 cm., exophoria 6Δ. She was able to fuse the Berens three-character test at 6.0 M. and 25 cm. On the orthoptoscope, there was an esophoria of 5Δ and second-grade fusion. She was able to abduct her right eye 40 degrees and her left eye 35 degrees.

CASE 6

B. D., a girl, aged 19 months, was first observed on May 5, 1947. Her parents noted that the infant's left eye turned in and never moved to the temporal side. In the family history there were two maternal uncles who had strabismus. There was nothing unusual in the patient's birth or medical history.

Examination. Both eyes were emmetropic under cycloplegia. Esotropia of 36 degrees was demonstrated by the Hirschberg test with the left eye deviating inward. The left eye could not be abducted beyond the midline.

A diagnosis was made of complete paralysis of the left lateral rectus.

Operation. On October 1, 1947, under general anesthesia, the left medial rectus was retroplaced 2.5 mm., the left lateral rectus resected 8 mm., and the vertical rectus muscles were transplanted. During the operation the following observations were made: The left medial rectus was bound down by adhesions to the sclera. The insertions of both vertical rectus muscles were very narrow, not more than 5.0 mm. in diameter.

On October 30, 1947, one month after operation, the patient was able to abduct the left eye to the lateral canthus. There was an esotropia of 16 degrees (Hirschberg test) at 6.0 M. When last observed, November 12, 1948, abduction of the left eye to the lateral canthus was performed with ease.

CASE 7

F. L., a man, aged 39 years, was first seen on December 13, 1940, through the courtesy of Dr. Daniel B. Kirby, with the complaint of diplopia following an automobile accident 10 months previously. The patient was a professional aviator and was anxious to join the Royal Canadian Air Force.

Examination revealed: vision, right and left eyes,

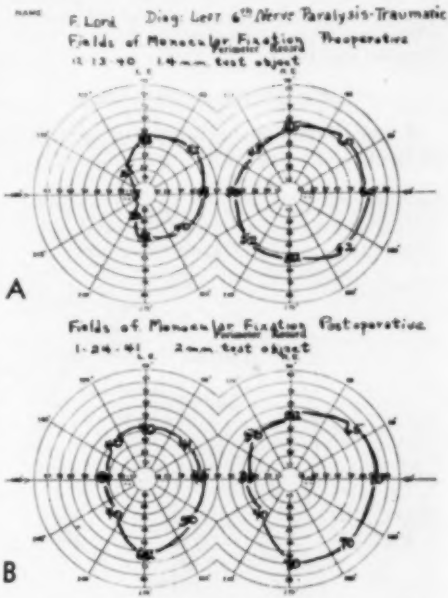


Fig. 5 (Berens and Girard). (A) Preoperative fields of monocular fixation of the left eye, Case 7. (B) Postoperative fields of monocular fixation of left eye, Case 7.

was 20/15 without correction. Accommodation was within normal limits. The eyes were normal except for esotropia of 40Δ at 6.0 M. and at 25 cm. Homonymous diplopia was revealed with the red glass and with the Worth four-dot test. There was second-grade fusion on the orthoptoscope with a 30 to 40Δ prism base out, but he was unable to fuse the three-character test. His error of refraction was insignificant.

Fields of monocular fixation (fig. 5a), using a 1.25-mm. object, were normal for the right eye but showed a limitation in the temporal field of the left eye. The patient could not abduct the left eye beyond the midline.

A diagnosis was made of complete paralysis of the left lateral rectus.

Operation. On January 10, 1941, the medial rectus was retroplaced 3.5 mm., the left lateral rectus re-

sected 8 mm., and the vertical rectus muscles of the left eye were transplanted. Two weeks later the patient was able to fuse the Worth four-dot test at 6.0 M. and 25 cm. and the three-character test. He had third-grade fusion. The field of monocular fixation showed a definite improvement over that recorded preoperatively (fig. 5b).

Six weeks after operation, the cover test revealed an esophoria of 10^{Δ} and left hyperphoria of 1.5^{Δ} at 6.0 M. He was able to maintain binocular single vision with the eye rotated 10 degrees to the left of the midline. Soon after his last visit he passed the physical examination for the Royal Canadian Air Force.

Summary and Discussion

A transplantation operation for paralysis of the lateral rectus, which not only utilizes the lateral halves of the vertical rectus muscles and the overlying Tenon's capsule, but also shifts the nasal halves of these muscles temporally to the vertical meridian, is described. Seven cases are reported.

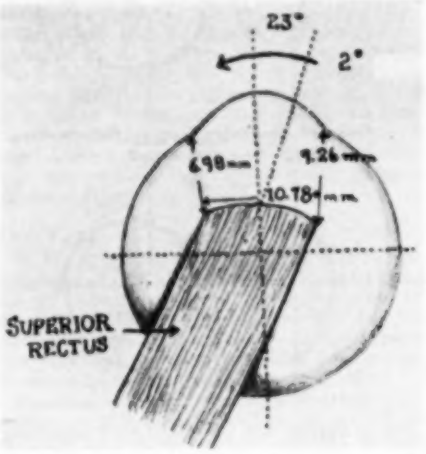


Fig. 6 (Berens and Girard). Normal average insertion of superior rectus with eyeball in primary position. Normal secondary action of the superior rectus is ADduction.

In all seven cases definite improvement in abduction and excellent cosmetic results were obtained. In two cases (1 and 7) third-grade fusion and in four cases (2, 3, 4, and 5) second-grade fusion were demonstrated on the orthoptoscope postoperatively. In only one case (4) was vertical imbalance revealed postoperatively which was not present preoperatively.

We believe that the satisfactory results can be attributed, in part, to attention to three points in the transplantation technique:

1. In addition to transplanting the lateral halves of the vertical rectus muscles and Tenon's capsule to the attachment of the paralyzed lateral rectus, the medial halves are transplanted to the lateral side of their insertions, thus converting the secondary action of the vertical rectus muscles from ADduction (fig. 6) to ABduction (fig. 7) in the primary position.

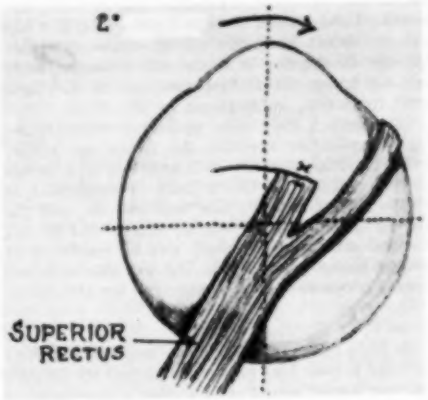


Fig. 7 (Berens and Girard). Following transplantation of the superior rectus, the secondary action of the superior rectus in the primary position becomes ABduction.

2. The medial rectus on the affected side is retroplaced whenever indicated at the time of transplantation. In our opinion reducing the action of the medial rectus contributed greatly to the degree of postoperative abduction obtained. Resection of a paralyzed muscle, even if augmented by transplanted slips of the vertical rectus muscles, usually does not produce a satisfactory functional result if the action of a strong, and often spastic, antagonist is not weakened.

3. Tenon's capsule, so far as possible, is left intact in this transplantation technique.

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References

1. Hummelsheim, E.: Weitere Erfahrungen mit partieller Sehnenuberpflanzung an dem Augenmuskeln. Arch. f. Augenh., **62**:71, 1908-1909; Zur partiellen Sehnenuberpflanzung am Auge. Ibid., **66**: 57, 1910.
2. Langdon, H. M., Ellis, V. M., and Mulberger, R. G.: Operative treatment of paralysis of the external rectus muscle. Arch. Ophth., **31**:254-255 (Mar.) 1944.
3. Reinhardt, P. H.: Correction of external rectus paralysis with contracture of the opposing internus. Am. J. Ophth., **27**:636 (June) 1944.
4. Mangus, J. S.: Congenital paralysis of both external recti treated by transplantation of eye muscles. Brit. J. Ophth., **28**:241 (May) 1944.
5. Gallo, E. A., and Novick, R.: Paralysis of external rectus. An. argent. de oftal., **6**:101-103 (July-Sept.) 1945.
6. Walker, J. P. S.: Operation for correction of paralytic external (lateral) rectus palsy. Brit. J. Ophth., **29**:477-479 (Sept.) 1945.
7. Lutman, F. C.: A tendon transplantation technique for external rectus paralysis. Am. J. Ophth., **29**:88-90 (July) 1946.
8. Berens, C., and Fonda, G.: Ocular sequelae of administration of general anesthesia. Arch. Ophth., **33**:385, 1945.
9. Berens, C.: Retroplacement for strabismus. Am. J. Ophth., **12**:720 (Sept.) 1929.

THE AMINO-ACID COMPOSITION OF THE PROTEINS OF THE OCULAR TISSUES

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The amino-acid composition of the proteins in the different tissues of the eyeball have been studied only in a limited number of investigations. The advent of the microbiologic assay methods made it desirable to reinvestigate these problems. Furthermore, the need for new data became apparent, notably in certain nutritional studies dealing with the metabolism of the eye, such as investigations of dietary inadequacies, especially amino-acid deficiencies.

In such investigations a series of ocular changes occur, the exact mechanism of which can be explained only on the basis of more complete knowledge of the biochemical composition of the ocular tissues. Such a case was the problem of the mechanism of the tryptophane deficiency cataract which, according to our findings (Schaeffer and Geiger), is explained by the inability of the body to synthesize protein from the available amino acids because one essential building stone of the protein molecule is lacking.

The intention of this paper was to reexamine and to compare the available data in successive steps by this newer method of investigation, anticipating in every further step new and probably unexpected problems which will again necessitate further research. In this first series of investigations the total undivided tissues of the cornea, sclera, and lens were examined and the resulting data were compared with those of other investigators, insofar as such a comparison was feasible.

The assay methods were essentially the same as those of Shankman, Dunn, and others. Nitrogen was determined by incomplete nesslerization. Conversion to the same percent total amino acids determined eliminates the possibility of nitrogen error from nesslerization. The data are presented on a 16-percent basis.

Amino-acid composition of the proteins of the cornea and sclera

The first nitrogen determinations in the sclera and cornea are described in the publications of Mörner, in 1894. He found that these tissues contain mainly collagen along

with a smaller quantity of mucoid. His surprisingly accurate analyses, for his time, were confirmed and completed by Jess, in 1923. Jess did not divide the different proteins, and made his analysis on the complete undivided material. The newest and most reliable investigations were accomplished by Krause, who completed the separation of the different proteins already attempted by Mörner. According to his analysis, the corneal and scleral tissues contain (besides a negligible amount of soluble proteins, albumin, and globulin) mainly mucoid, collagen, and also a third protein, elastin. The amino acids determined in the investigations of Krause were cystine, histidine, lysine, tryptophane, and tyrosine. The qualitative analysis of arginine, histidine, and lysine were carried out by the Van Slyke method; the data on the other amino acids were obtained by colorimetric methods.

It is evident that, while there is little possibility of comparing the data of Krause with our results, the data of Jess, on the other hand, are accessible for such a comparison. But even considering all data in the existing literature, it is obvious that the total information available is, as yet, insufficient since the number of the investigated amino acids is incomplete.

The results are summarized in three tables.

Table 1 shows the relative amino-acid content of the cornea and the sclera. These data coincide only partly with the data given by Jess, necessitating further analysis. The values concerning the three amino acids determined by Jess, compared with the values obtained in our investigation, are not too different; while there is a considerable divergence in the results concerning especially lysine. This is the more remarkable since the lysine values in the cornea, as well as in the sclera, are equal according to our analysis, namely 3.8 percent, and in the investigation of Jess they are highly discordant. He obtained 5.52 percent for the cornea and 11.56 percent for the sclera. These contradictory data need clarification (table 2).

Special consideration has to be given to the relative values of the three amino acids in Table 1. The histidine, lysine, and arginine disclose a familiar relationship. These amino acids have been found in a similar relationship in a protein arbitrarily called eukeratin, which was defined as an insoluble

TABLE 1

AMINO ACIDS IN HUMAN CORNEA AND SCLERA PROTEINS (N×6.25)

	Schaeffer and Shankman		Jess	
	Cornea	Sclera	Cornea	Sclera
	%	%	%	%
Arginine	7.6	7.6	5.51	2.90
Aspartic acid	7.4	6.6		
Glutamic acid	11.0	10.8		
Glycine	18.0	17.5		
Histidine	0.71	0.81	0.99	0.78
Isoleucine	3.0	2.4		
Leucine	4.7	4.0		
Lysine	3.8	3.8	5.52	11.56
Methionine	1.1	1.2		
Phenylalanine	2.9	2.3		
Serine	4.3	3.8		
Tyrosine*	1.4	1.3		
Threonine	2.8	2.7		
Valine	3.8	3.7		

* Low due to presence of carbohydrate and acid hydrolysis.

protein resistant to enzymatic digestion which yields histidine, lysine, and arginine in the molecular ratio of approximately 1:4:12.

Eukeratins have been found in human, cattle, camel, and chimpanzee hair, in fingernails, cattle horn, lamb wool, and so forth.

Table 3 compares our analytical data with a few data showing the amino-acid composition of eukeratins analyzed by Block, namely human hair, fingernail, and cattle horn. Evidently the cornea and the sclera contain the three amino acids—histidine, lysine, and arginine—in the characteristic relationship already mentioned; that is, approximately 1:4:12.

With regard to these data, these ocular tissues might be considered as mainly eukeratinoid in structure. Of course, this statement is aforehand arbitrary, as only similar findings after separation of the different proteins can justify it.

Our analysis also revealed a high glycine content of the cornea and the sclera.

The amino-acid composition of the cornea and the sclera reveals a great similarity, although some differences were found, especially in the values of leucine, isoleucine, and phenylalanine, which may possibly be significant but cannot be so claimed with the limited data.

TABLE 2

COMPARISON OF OUR DATA CONCERNING HISTIDINE, ARGININE, AND LYSINE OF THE CORNEA AND SCLERA WITH THE DATA OF JESS

	Cornea		Sclera	
	Jess	Schaeffer and Shankman	Jess	Schaeffer and Shankman
Histidine	0.99	0.71	0.78	0.81
Arginine	5.51	7.6	2.90	7.6
Lysine	5.52	3.8	11.56	3.8

TABLE 3

COMPARISON OF EUKERATINS WITH CORNEA AND SCLERA

	Histidine	Lysine	Arginine	Ratio
	%	%	%	
Cornea	0.71	3.8	7.6	1:5:10
Sclera	0.81	3.8	7.6	
Human hair	0.6	2.5	8.0	1:4:13
Fingernails	0.5	2.6	8.5	1:5:17
Cattle horn	0.6	2.5	8.6	1:4:14

AMINO-ACID COMPOSITION OF THE PROTEINS OF THE CRYSTALLINE LENS

The exact chemical composition of the tissue proteins of the crystalline lens has been the subject of several investigations. The earliest analyses were those of Mörner, whose findings were largely confirmed by Jess. Jess divided the lens proteins in α- and β-crystallins and albuminoid and analyzed them for 15 amino acids.

A more recent analysis was furnished by Krause, who isolated more meticulously the individual lens proteins. His amino-acid determination was, however, limited to the analysis of tryptophane, cystine, arginine, histidine, lysine, and tyrosine.

A more recent study of the composition of the total proteins of sclerosed and cataractous lenses by Bloch and Salit determined nine amino acids. These investigators used chemical methods for tyrosine, tryptophane, phenylalanine, cystine, and methionine. Ly-

sine, leucine, isoleucine, and valine were estimated by microbiologic techniques.

The results of the amino-acid estimations in the total lens proteins by the microbiologic assay method is given in Table 4. We analyzed lenses of steer, hog, calf, and man. Normal, as well as cataractous, human lenses have been investigated. The outstanding features of this analysis are tabulated and our results can be summarized as follows:

1. Fourteen amino acids have been determined. Of these, 10 coincide with the data of Jess. We have assayed, in addition to nine amino acids determined also by Jess, leucine and isoleucine separately, and also serine, threonine, and methionine.

A comparison of our results with the data of Jess is of restricted value, since his analysis involved separation of three different proteins. While such a comparison is greatly arbitrary, it is still revealing. Inadmissible is a comparison with the data of Krause. On the other hand, a direct comparison with the values of Bloch and Salit is justified. These investigators analyzed the undivided normal and cataractous lens, and data of eight amino acids coincide with our data. Table 5 gives the data of Jess and Bloch and Salit compared with our values.

2. An interesting finding in our investigation is that the lens of the human eye contains significantly less histidine and significantly more leucine and isoleucine than the lens of the other examined animals.

3. No significant differences were found in the amino-acid composition of the normal and the cataractous human lenses.

4. In our studies the values for leucine, isoleucine, phenylalanine, aspartic acid, serine, and valine are particularly higher than previously reported, while our values for arginine and histidine are not far from those reported by Jess. The glutamic-acid content we found to be somewhat higher than the value reported by Hijikata, but it is considerably higher than the value given by Jess. All our data, when they coincide, are in a very close agreement with those given by

TABLE 4

AMINO ACIDS IN LENS PROTEINS* ($N \times 6.25$)

	Human					Steer	Hog	Calf	Mean Human	Mean Animal
	#1	#2	#3	#34	#24	#27	#30	#33		
	Cataract	Cataract	Diabetic	Normal	Normal	Normal	Normal	Normal		
Arginine	10.9	10.4	11.2	11.9	11.0	11.1	11.6	11.2	11.1	11.3
Aspartic acid[b]	9.7	10.2	10.4	9.4	9.8	9.6	9.6	10.4	9.9	9.9
Glutamic acid	—	13.7	14.8	16.2	16.5	15.7	16.8	15.0	15.3	15.8
Glycine	4.5	4.6	4.8	4.8	5.2	5.1	5.9	4.8	4.8	5.3
Histidine	3.6	3.5	4.0	4.0	3.7	4.7	4.8	4.9	3.8	4.8
Isoleucine	6.6	6.9	6.8	5.8	6.1	5.7	5.2	5.6	6.4	5.5
Leucine	9.2	9.4	9.2	8.2	8.8	8.0	7.8	8.1	9.0	8.0
Lysine	5.2	5.8	6.0	5.7	5.2	5.1	5.0	5.6	5.5	5.2
Methionine	3.2	3.2	2.9	2.5	2.8	2.2	2.5	2.4	2.9	2.4
Phenylalanine	8.0	8.8	7.8	8.7	9.2	9.1	8.3	9.2	8.5	8.9
Serine†	7.7	8.4	8.1	7.2	6.0	7.8	7.7	7.8	7.5	7.8
Tyrosine[a]	7.7	7.5	6.4	7.4	7.9	6.8	6.8	6.8	7.4	6.8
Threonine[b]	3.6	3.7	3.3	4.4	4.1	4.8	3.3	4.1	3.8	4.1
Valine	5.5	5.5	5.6	4.8	5.1	5.4	6.1	5.6	5.3	5.7

* Corrected to the same total percent amino acids determined (101.3%), which was mean after omitting one value which was obviously in error due to nitrogen.

† Unpublished method. *L. mesenteroides*.

[a] Minimal values, due to acid hydrolysis.

[b] Variation of samples may be assay error, not sample variation.

[c] Hac and Snell method.

Bloch and Salit (valine, leucine, isoleucine, tyrosine, phenylalanine, lysine, and methionine).

Serine, which we found to be present in the amount of 7.6 percent on the average, was reported by Jess as "traces."

The greatest discrepancy between our results and those of previous workers has to do with glycine, which we found in the amount of 5.0 percent and which Jess and also Hijikata reported to be totally absent; a finding in line with low glycine values by early colorimetric or Fischer ester methods.

TABLE 5

COMPARATIVE TABULATION OF THE AMINO-ACID VALUES IN MAMMALIAN LENSES

Amino Acids	Albuminoid	Jess		Bloch and Salit	Our Data
		α—Cryst.	β—Cryst.		
Glycine	0	0	0		4.5– 5.9
Alanine	0.8	3.6	2.6		
Valine	0.2	0.9	2.1	5.2	5.1– 6.1
Leucine				7.3–7.5	7.8– 9.4
Isoleucine	5.3	5.7	2.8*	6.2	5.2– 6.9
Aspartic acid	0.5	1.2	0.4		
Glutamic acid	4.6	3.6	2.7		13.7–16.8
Tyrosine	3.6	3.6	3.7	6.0	6.4– 7.9
Proline	1.9	1.8	1.4		
Phenylalanine	4.6	5.5	4.1	8.5–8.8	7.8– 9.2
Lysine	3.87	3.83	4.6	6.0	5.1– 6.0
Histidine	2.73	3.81	3.59		3.5– 4.9
Arginine	10.26	8.0	7.43		10.4–11.9
Cystine	3.1	2.3	4.9	1.5	
Serine					6.0– 8.4
Tryptophane				3.3–3.4	
Methionine				3.5–3.8	2.2– 3.2
Threonine					3.3– 4.8

* Both amino acids were determined together.

COMMENTS

The present investigation attempted to add new data to our incomplete knowledge of the amino-acid composition of the ocular-tissue proteins, that is of the cornea, sclera, and of the crystalline lens. The limitations in the usefulness of the obtained data are obvious. Neither complete separation of the different tissues was attempted nor were the different proteins isolated. The investigation involved the whole tissues. Thus the comparative evaluation of the obtained data is restricted to those earlier investigations accomplished with similar presumptions and aims.

From Tables 1 and 5 it is seen that the number of amino acids for which analytical information is available is increased by the present paper. This is more true concerning the corneal and scleral tissues which were, as yet, only poorly investigated. The estimation of the following amino acids is, as yet, wanting in our investigations: tryptophane, cystine, alanine, proline, and hydroxyproline. On the other hand, the investigations furnished several completely new data.

One item in our findings, as already emphasized, needs further investigation, namely, the conjecture of the keratinoid nature of the corneal and scleral tissues. This would be more remarkable since keratin, commonly found in epithelial structures, has never been demonstrated as a constituent in ocular tissues, except as neurokeratin, in the framework of the retinal tissue (Krause).

Investigations of this kind seem to us to be interesting since they might supply a closer understanding of physiologic and pathologic processes on a biochemical basis. On the other hand, information obtained by these investigations is not exhausting the un-

derlying problems and that of different reasons. It is not satisfactorily established to what extent the quantity of the individual amino acids in the hydrolysate is identical with the amount present in the proteins analyzed before hydrolyzation. The data are only approximations, even if very close ones, and we do not exactly know the amount destroyed in the process of hydrolysis. There are no perfectly accurate methods of estimation as yet, although the microbiologic assay method signifies an enormous advance; but even this method is not applicable to the investigation of all known amino acids (Geiger).

Of great advantage for these studies would be the parallel and combined investigation with the methods of chromatography and X-ray studies (Astbury), which might furnish more information about the submicroscopic architecture of the protein molecule.

Our findings have thus many limitations and they are intended only as a preliminary study for an experimental approach of other related problems.

Summary

1. The amino-acid composition of the total proteins in the corneal and scleral tissues were analyzed by the microbiologic assay method. Fourteen amino acids were determined. As a result of this analysis the cornea and the sclera are probably eukeratinoid in composition. Normal and pathologic lenses did not differ significantly in composition.

2. The amino-acid composition of the total proteins in normal and cataractous lenses in humans and in normal lenses of other mammals (steer, hog, and calf) were analyzed by the same method of microbiologic estimation. Fourteen amino acids were determined, accounting for nearly 100 percent of the total nitrogen. The data thus obtained show several discrepancies with similar data obtained by chemical methods.

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References

Astbury, W. T.: Röntgenologische Untersuchungen von Naturstoffen. In: E. Bamann and K. Myrbäck: Die Methoden der Fermentforschung. New York, Academic Press, 1945.

Bloch, R., and Salit, P. W.: A note on the amino acids of cataractous and sclerosed human lenses. Arch. Biochem., **10**:277, 1945.

Block, R. J., and Bolling, D.: The composition of the keratins: The amino acid composition of hair, wool, horn, and other eukeratins. J. Biol. Chem., **128**:181, 1939.

Geiger, E.: Biochemistry of fish proteins (in print).

Hijikata, Y.: On the cleavage products of the crystallin lens. J. Biol. Chem., **51**:155, 1922.

Jess, A.: Die moderne Eiweisschemie im Dienste der Starforschung. Graefe's Arch. f. Ophth., **109**: 463, 1922.

———: Zur vergleichenden Chemie der Hornhaut und der Lederhaut des Auges. Graefe's Arch. f. Ophth., **112**:489, 1923.

Krause, A. C.: The Biochemistry of the Eye. Baltimore, Johns Hopkins Press, 1934.

———: The chemical constitution of the sclera. Arch. Ophth., **7**:598, 1932.

———: The chemistry of the sclera. Am. J. Ophth., **16**:214, 1933.

———: Chemistry of the lens: I., Arch. Ophth., **8**:166, 1932; II. ibid., **9**:617, 1933; III. ibid., **10**:631, 1933; IV. ibid., **17**:502, 1934.

Mörner, C. T.: Untersuchung der Proteinsubstanzen in der lichtbrechenden Medien des Auges. I. Ztschr. f. physiol. Chem., **18**:61, 1894; II. ibid., **18**:213, 1894; III. ibid., **18**:233, 1894.

Schaeffer, A. J., and Geiger, E.: Cataract development in animals with delayed supplementation of tryptophane. Proc. Soc. Exper. Biol. & Med., **66**:309, 1947.

Stern, E. and Shankman, S.: In preparation.

CATARACT DISCISSION OPERATIONS*

An experimental evaluation

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A study of the comparative techniques of this surgical procedure is essentially a review of the varied principles of the operation itself. The discission operation may be classified into four major groups according to the type of entrance made into the lens capsule:

1. Incision through the anterior lens capsule.
2. Discission extending through the cortex and nucleus of the lens.
3. Through and through discission penetrating the entire lens and traversing the hyaloid membrane into the vitreous.
4. Discission by first entering the posterior lens capsule by a penetration behind the ciliary body.

The technique classified in Group 4, though advocated and used only a few times, is not included in this study. Because it disturbs the ciliary body and poses technical difficulties, as well as being a potential source of uveitis, it is not considered of sufficient merit to warrant use in these experimental studies.

Discission operations of the four major groups were performed on 24 rabbit† eyes. Postoperative follow-ups were conducted daily for one month. At the end of that period, the animals were killed, and the eyes were examined for all changes that had occurred during that period. The techniques used were selected because they embodied all of the principles outlined in the ophthalmic literature. It was believed that this study would answer questions of efficacy posed by various writers, would demonstrate whether the techniques were based on physiologic fact, and would provide an opportunity to analyze any secondary or side reactions that might occur.

Details of study

Fourteen rabbits were used for this test. Two of the rabbits, used as controls, were examined to ascertain what constituted a normal rabbit lens. Measurements in four rabbit lenses were: anterior-posterior: 9.3, 9.3, 9.0, 8.9 mm.; lateral: 11.4, 11.3, 11.4, 11.2 mm.

The five techniques employed were: (1) Transverse incision through the anterior capsule; (2) anterior cross incision, rupturing the lens capsule and extending half-way through the nucleus; (3) inverted V-shaped incision of Ziegler, through and through; (4) through and through cross incision; (5) mixed incision, through and through.

Preoperative studies

1. Cultures were made from each rabbit eye. Blood-agar plates were used and the results were observed 48 hours later.
2. Preoperative tension (Schiøtz) was taken.
3. External and funduscopic examinations were made.
4. Sterilization of operative field was done.

Postoperative studies

1. Tensions‡ (Schiøtz) were taken pre-

* Thesis for Master of Science in Ophthalmology from the Graduate School of Medicine of the University of Pennsylvania.

† Virgin rabbits, four to five months old, were used in these studies.

‡ B. Y. Alvis (1921) is cited by Ziegler (1925) for studies of tensions following discission operations. The conclusions are noted as:

1 (8 animals). Shallow incision, anterior capsule (3 mm. long), few anterior fibers. No reaction, no change in tension; wound healed with small scar on front of lens.

2 (13 animals). Large shallow incision, in some two incisions, across the front of the lens, but in-

operatively and postoperatively for four days and on the 10th day postoperatively.

2. Slitlamp examinations were made.

3. Daily progress or the reactions of the techniques used was noted.

4. Dilatation of the pupils was effected by daily instillation of one-percent atropine ointment.

5. Final dissection and evaluation were done on the 28th postoperative day.

Instruments and operative procedure

Each rabbit was wrapped in a sheet with only the head exposed. Three to four minutes before surgery, 4 to 6 drops of one-percent pontocaine were instilled into each eye. The lids remained opened without the use of a retractor, and the insertion of the superior rectus muscle was grasped with a fixation forceps and held while the Ziegler knife-needle was inserted into the eye at the corneoscleral junction just at the limbus.

TABLE 1

Tension readings in eyes of rabbits in Group I (in mm. Hg (Schiøtz))

Rabbit Eye	Perop.	1st Postop. day	2nd	3rd	4th	10th
1	17	17	14	13	16	14
2	16	16	16	16	15	16
3	16	18	15	15	17	16
4	17	18	17	15	16	15

The animals operated were grouped according to the five discission techniques, already described, which were used in this study. Each group was followed during the entire observation period of one month.

Results

Group I

Anterior capsule linear discission, rupturing the anterior capsule (fig. 1). A single anterior transverse incision was made on the four eyes in this group, just deep enough to reach the central nucleus of the eye. Preoperative and postoperative tension readings are listed in Table 1.

A transverse linear opacity was observed 24 hours postoperatively with a little iris reaction of margin hyperemia. The anterior chamber was clear and of normal depth. The cornea remained clear.

The 2nd and 3rd days showed continued opacity except in No. 4 eye in which little change was noted. This was verified under slitlamp examination. In eyes No. 1, No. 2, and No. 3, a central haze of the lens developed which, under slitlamp examination, revealed an opacity of the nucleus with noticeable change of the refraction of the light beam in the other portion of the lens. No. 4 eye showed only a linear streak of the old discission site, and no further change was noted at any time.

There was only a slight hyperemia of the iris, and this for the most part subsided by the eighth day.

The anterior chamber and cornea remained clear and during the third week the anterior chamber appeared a bit deeper. When seen with a slitlamp at this period, the hazy nucleus (except No. 4) of the lens seemed to be more anterior, and there was a thinning of the anteroposterior diameter to a slight degree.

On the 28th postoperative day, each lens was removed and showed a slight thinning of the cortex with little or no nuclear change. No. 4 eye showed no change except the scar on the anterior capsule, as seen on slitlamp examination. Figure 1-a shows the average changes that took place in the lenses of this group during the 28-day period.

cluding capsule and few anterior layers of lens cortex. Five showed no increase in tension, six showed definite increase in tension in 1 to 7 days.

3 (5 animals). Narrow incision made entirely through the lens. Three showed no tension changes. One had a marked, violent reaction.

4 (5 animals). Complete discission was made of these. Four showed moderate decrease in tension, which persisted for two weeks. One showed slight increase. There was a moderate reaction in all of these cases and immediate clouding of the entire lens, which proceeded to absorption in all animals which were permitted to live long enough.

The nucleus of the lens was slightly opaque in eyes No. 2 and No. 3, with less in No. 1. There were no changes in eye No. 4.

A slight liquefaction of the lens cortex was present about the nucleus, which was placed a bit forward by the absorption of the cortical material and a decrease in the anteroposterior diameter.

The hyaloid remained intact in each eye, and the vitreous was clear. No change was noted in the fundi on the 28th day.

This group did not demonstrate any conjunctival or ciliary injection.

GROUP II

Anterior cross incision, rupturing the lens capsule and extending halfway through the nucleus (fig. 2). A penetration was made sufficiently deep to include the nucleus. There were six eyes in this group. Tension readings are given in Table 2.

Very little opacity was noted 24 hours postoperatively; however, some generalized iris hyperemia was evident. In this group, the lens opacity was more in the anterior half. It first started at a central position. In eyes No. 5 and No. 7, lens material was in the anterior chamber on the eighth postoperative day, with eye No. 5 showing complete lens opacity on the 10th day. The lenticular changes were diffuse in type, with the central section being of greater density and clearer at the equator. This did not vary except in eye No. 5.

Fig. 1-a (Raiford). Lateral view showing slight absorption and degeneration of the anterior half of the lens cortex; no nuclear involvement.

Fig. 1 (Raiford). Anterior capsule transverse linear discission not extending to nucleus. (The nucleus is darkened in these drawings to demonstrate better contrasts.)

TABLE 2

TENSION READINGS IN EYES OF RABBITS IN GROUP II
(in mm. Hg (Schiøtz)

Rabbit Eye	Preop.	1st Postop. Day	2nd	3rd	4th	10th
5	18	17	17	18	17	17
6	18	16	17	18	18	16
7	17	19	17	17	17	15
8	18	18	18	16	17	15
9	14	17	20	18	18	16
10	15	17	19	18	18	17

Fig. 2 (Raiford). Anterior cross discission of lens cortex extending into the nucleus.

On the 18th postoperative day, eyes No. 7 and No. 8 were dissected to study the progress of lenticular absorption. A gradual or slight increase of depth of the anterior chamber was present under the slit-lamp.

Fig. 2-a (Raiford). Lateral view showing anterior cortex absorption and decrease in lens thickness.

There was postoperative hyperemia in each eye of this group. In eye No. 7 a posterior synechia was present at the 10-o'clock position on the lens and there was vascularization of the iris in that segment.

On the 18th day, eyes No. 7 and No. 8 were examined. The lens nucleus was opaque in each with liquefaction of the remainder of the lens cortex which, at this time, was only about two thirds of its normal thickness.

On the 28th day, eye No. 5 was almost completely absorbed, except for a small portion of the nucleus. Eyes No. 6 and No. 9 revealed liquefaction of the cortex (fig. 2-a) except the nucleus, which was about half size. Eye No. 10 showed the nucleus partially protruding through the incision of the anterior capsule which was impeding the rate of cortex absorption.

There was some increased ciliary injection in eye No. 5, with only a slight amount in the remainder of the group at the end of the first postoperative week. This gradually decreased and was only slightly evident on the 24th day.

The corneas were clear in each eye of this group.

The hyaloid membrane, vitreous, and retinas were normal on ophthalmoscopic examination. The iris in each eye was hyperemic and remained so throughout the period of observation. Only in eye No. 7 did synechia occur.

Group III

Ziegler inverted-V through and through discission technique (fig. 3). Four eyes were studied in this group. Tension readings for this group are listed in Table 3.

The lens was opaque at the end of the first 24 hours, postoperatively, in the central portions. The anterior chambers were of normal depth. In eye No. 12, a small hyphemia was noted in the anterior chamber. The lenticular opacity progressed and, by the end of the

sixth postoperative day, each lens of this group was totally opaque.

There were changes in the cornea in this group.

Hyperemia and periciliary injection were present in each eye, and extended to involve an area of three mm. about the limbus and gradually faded toward the periphery of the bulbar conjunctiva.

The anterior chamber of each eye remained clear, except for lens material and the hyphemia in eye No. 12. This was absorbed by the eighth postoperative day. In eye No. 11 the lens material which had filled the central third of the anterior chamber

TABLE 3

TENSION READINGS IN THE EYES OF RABBITS IN GROUP III
(in mm. Hg (Schiøtz))

Rabbit Eye	Preop.	1st Postop. Day	2nd	3rd	4th	10th
11	18	19	24	25	25	17
12	16	19	22	24	20	18
13	17	24	24	24	17	19
14	18	24	22	17	18	18

gradually decreased in volume on the 16th postoperative day, and on the 28th day only the nucleus remained, which was less than half size.

The iris in each of the eyes manifested marked hyperemia, which only subsided to a slight degree from the period of the 16th to the 20th day. Under slitlamp examination, there was engorgement of the iris vessels, and in No. 14 neovascularization was seen scattered in the upper portion. In No. 13 a firm posterior synechia was attached to the anterior lens capsule and was not broken by one-percent atropine or neosynephrine emulsion (10 percent).

From the 20th day the anterior chambers appeared deeper than normal, which was revealed to be due to lenticular absorption at the time of dissection on the 28th day.

On the 28th day the lenses were found to be from 60 to 75 percent absorbed (fig. 3-a).

Fig. 3 (Raiford). Inverted-V through and through discission.

The lens capsule showed evidence of shrinkage which was, no doubt, due to loss of cortex. The lamellas of each lens were liquefied and, on cutting away the iris, much

Fig. 3-a (Raiford). Lateral view showing anterior protrusion of nucleus with synechia on posterior lens capsule with adhesions extending into vitreous space.

Fig. 4 (Raiford). Through and through cross incision penetrating the nucleus into the vitreous.

of this liquefied lens substance escaped about the central nucleus, which in itself was absorbed to about two thirds to one half and

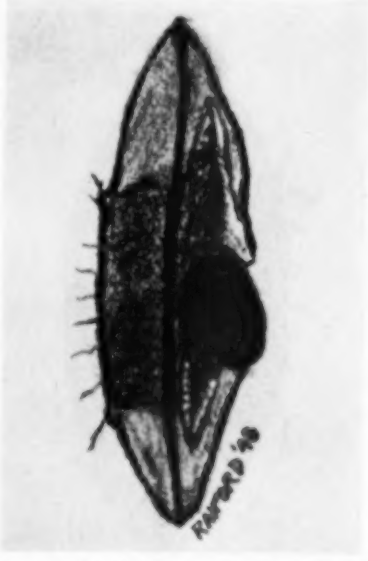

Fig. 4-a (Raiford). Lateral view. Complete degenerative changes of the entire lens with absorption of lens nucleus; numerous fibrous bands extending into the vitreous space.

caught in the anterior discission aperture of the capsule. When the lens nucleus was removed, the posterior perforation was seen and, in each eye of this group, adhesions existed between the posterior lens capsule and that of the hyaloid membrane. There was a small amount of fibrous material extending into the vitreous just posterior to the hyaloid adhesion for a distance of 1.0 to 2.0 mm. and about 2.0 to 2.5 mm. in diameter. A small segment of this anterior vitreous in this area appeared to be liquefied.

The vitreous and fundi remained clear throughout in eyes of this group.

GROUP IV

Through and through cross incision was made with the pupil dilated and the knife

TABLE 4

TENSION READINGS IN THE EYES OF RABBITS IN GROUP IV
(in mm. Hg (Schiøtz))

Rabbit Eye	Preop.	1st Postop. Day	2nd	3rd	4th	10th
15	16	22	22	22	20	16
16	18	22	20	22	20	17
17	18	22	21	20	21	18
18	20	22	20	20	20	18

needle penetrated into the vitreous (fig. 4). Four eyes were in this group. Tension readings appear in Table 4. Since the basic difference in the technique used on this group, compared to Group III, was only in that the incision was the cross type, through and through, the eyes in this group reacted essentially as the eyes in Group III.

The reaction of the perilimbal area was moderate, and there was a gradual increase in severity of ciliary injection from the 1st to the 6th postoperative day. This began to subside on the 11th day, but remained injected throughout the duration of the 28-day period.

The cornea was clear except in eye No. 17 in which some lens fragments were in the inferior portion of the anterior chamber.

There was some opacity of stroma at this segment.

The iris was hyperemic on slitlamp examination with marked increase of vascularization in eyes No. 16, No. 17, and No. 18. There were several transitory posterior synechias which were broken up by mydriatics. This congestion persisted throughout the 28-day period, although it leveled off during the last week.

The anterior chambers were clear except the portion taken up by lenticular fragments, which protruded into the center part with eye No. 17 extending to the lower half.

The lenses were centrally opaque and grossly dense involving about 80 percent of their total volume. The nucleus (fig. 4-a) protruded forward with almost complete liquefaction of the cortex.

In each case the hyaloid membrane was adhered to the posterior lens capsule with a small area of liquid vitreous extending beyond this region. Some irregular proliferation of fibrous material was evident here. In eye No. 18 a fibrous vitreous band extended from the hyaloid adhesion at the posterior capsule to the retina just anterior to the equator at the 10-o'clock position, creating a retinal detachment in this area of a bulbous type. The detachment was about 3 to 4 mm. in diameter and slightly elevated. This was first seen when the iris was removed at the ciliary body on the 28th postoperative day. No noticeable change in the dissection (28th day) technique was noted that could be responsible for the detachment. Retinas of the three other eyes were clear.

GROUP V

Mixed discission, through and through penetration of the lens (fig. 5). Six eyes were used for this group. Tension readings are shown in Table 5.

This group showed the greatest over-all postoperative reactions. No. 11 (eyes No. 21 and No. 22) died on the third postoperative day and dissection of the eyes showed marked iris congestion with small hemorrhagic petechias on the posterior surface, greater near the pupillary zone. The lenticu-

Fig. 5 (Raiford). Multiple through and through discissions of the entire lens and nucleus extending into the vitreous.

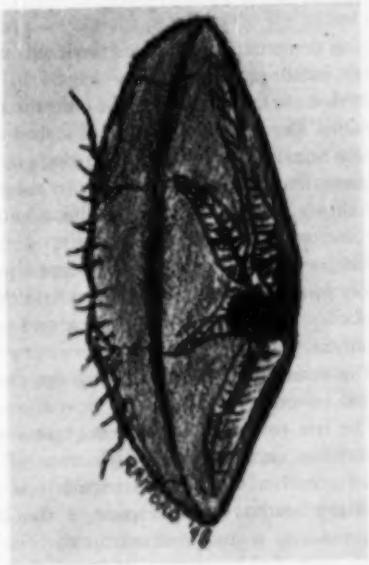

Fig. 5-a (Raiford). Lateral view. Marked absorption of lens, cortex, and nucleus with multiple fibrous bands extending into the vitreous space and flattening of the lens.

lar changes revealed generalized opacity with beginning degenerative changes in the lens cortex.

Eye No. 23 developed uveitis and precipitates covered the lower half of the corneal endothelium. They were lobulated in shape and under slitlamp examination appeared to have a dull gray color. No aqueous flare was seen. The iris of this eye developed pigmentary degeneration after five days of hyperemia and congestion. On the 28th day dissection demonstrated a thin, friable iris with many small petechial hemorrhages on the posterior surface and synechia onto the lens capsule. The lens was greatly absorbed and totally liquefied with a brownish tinge to the degenerative liquid vitreous in the anterior two thirds, with the posterior portion having gel-like qualities.

TABLE 5

TENSION READINGS IN THE EYES OF RABBITS IN GROUP V
(in mm. Hg (Schiøtz))

Rabbit Eye	Preop.	1st Postop. Day	2nd	3rd	4th	10th
19	17	20	22	21	22	19
20	17	20	21	22	20	17
21	14	22	22	—*	—	—
22	15	22	22	—	—	—
23	17	19	19	18	19	16
24	16	18	20	18	18	17

* Animal died on the third postoperative day.

The remaining three eyes developed perilimbic injection, being marked the first three weeks by hyperemia of the sclera and conjunctiva.

The corneas were clear during the entire period of observation.

The iris revealed marked congestion and hyperemia on slitlamp examination. Posterior synechias developed irregularly at the pupillary border. On dissection at the 28th day, vascular tortuosities were clearly scattered over each posterior iris surface in a generalized pattern.

Each lens of this group developed a total opacity with complete liquefaction of the cortical material, and only a small portion of the nucleus remained on the 28th day (fig. 5-a). The posterior capsules had massive adhesions to the hyaloid membrane and numerous fibrillar strands extended out into the vitreous. The lenticular absorption was greatest here, less than one fourth of the total lens volume remaining. The posterior capsule was opaque.

The vitreous showed liquefaction on the portion next to the lens.

The retinas were clear throughout, with no loss of sheen or pigmentation.

SUMMARY OF EXPERIMENTAL DATA

A review of the five different cataract discissions which include the major mechanisms underlying the various techniques of this operation shows:

Bacteriology. All preoperative cultures contained only Staphylococcus albus.

Tension. A Schiøtz tonometer was used, by which tensions were taken preoperatively, during the first four postoperative days, and on the 10th postoperative day. The average preoperative reading was 17 mm. Hg. No change was noted in Groups I and II. In Group III there was a slight postoperative rise which was present on the 2nd and 3rd day, being greater on the fourth. These tensions returned to preoperative levels by the 10th day. Groups IV and V developed a higher postoperative tension elevation, which returned to normal on the 10th day. These tension curves may be considered to be within normal limits.

Perilimbal area. Groups III, IV, and V showed the greatest periciliary injection, Group V showing the most marked reaction. The congestion and hyperemia persisted into the third week in Groups III and IV, and during the entire period for Group V. In Groups I and II only a transitory injection was evident, which disappeared during the first week.

Cornea. The cornea remained clear in all except eye No. 23, in which uveitis developed. With the use of one-percent pontocaine as a local anesthetic, a mottledlike change occurred in the epithelium. On view-

ing the cornea with a plus 10D. lens, minute facets were produced, which on illumination created shadows on the iris. These disappeared in 24 hours.

Iris. The only change in the iris was that of hyperemia and congestion (except in eye No. 23) in Groups I and II, with some increase in Group III. Groups IV and V developed more marked congestion with tortuosity of the vessels which persisted throughout the 28-day period, and in Group V posterior synechias developed.

Anterior chamber. Other than lenticular fragments and one case of hyphemia (eye No. 12), the anterior chambers remained clear.

Lens. Only one lens (eye No. 4) failed to develop any process of absorption. The least reaction was in Group I. Group II revealed a steady lenticular absorption with cortical liquefaction. The nucleus was still firm, though smaller than normal on the 28th day. Groups III and IV showed essentially the same changes, but slightly more advanced; these two groups developed hyaloid-membrane adhesions and, in one case (eye No. 18), a vitreous band which produced traction was responsible for a retinal detachment. The vitreous adjacent to the hyaloid was involved by liquefaction. Illustrations indicate the varied contours of the lenses at the time of dissections on the 28th postoperative day.

Group V developed the greatest lenticular reaction, synechias were more severe, and more degeneration of the lens and cortex existed. The nucleus of the lens was smaller or failed to exist. This group revealed the most lenticular absorption that produced complications not evident in the other groups. The posterior capsule showed more hyaloid adhesions and involvement of the vitreous proper.

Conclusions

1. Very little change in tension was noted in Groups I and II. Groups III, IV, and V showed changes in postoperative tension levels during the first four days. Although tensions in all groups were within normal limits on the 10th day, the fluctuations of elevation after operation should cause close scrutiny of the techniques used in the last three groups of this study.

2. The single transverse discission (Group I) through the anterior lens capsule proved to be insufficient and, in order to obtain a more rapid lenticular absorption, the technique would have to be repeated as clinically indicated.

3. The cross anterior capsular discission (Group II) gave a more rapid lenticular absorption with a slight reaction to the anterior uveal tract. No involvement of the hyaloid membrane or vitreous was represented in this group. This technique appeared to be the best of any in the series, and indicated that a cataract discission which involves the anterior capsule to or through the lens nucleus is the best of any demonstrated in this experimental evaluation. There were fewer side reactions and this technique would seem to be the one of choice. It should prove to be the safest and give the best end results.

4. The through and through techniques, as the Ziegler (Group III) and cross incision (Group IV), gave a more rapid lenticular absorption. They also developed the complications of hyaloid membrane and posterior capsule adhesions in each case, as well as degenerative vitreous changes. In one case a vitreous-band adhesion was responsible for a retinal detachment. In Group V the same method was used to complete lenticular penetration with more maceration of the lens substance. Here complications were more severe. Its only advantage was that of more rapid lens absorption.

Because of the side reactions and complications demonstrated by the through and through technique, it is not considered to be a safe procedure and is not based on sound surgical principles. These studies would suggest that it be discarded as a method of cataract discission operation.

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RECENT CANCER RESEARCH AND ITS RELATION TO OPHTHALMIC PROBLEMS*

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The curious dichotomy between general pathology and ophthalmic pathology, which existed at the beginning of the century but which fortunately is fast disappearing, had some disadvantages for the ophthalmologist but certainly more for the general pathologist. He usually remained unaware of the unique conditions existing in the eye and of the highly specialized and unusual ways in which it is affected by malignant disease. The study of ophthalmic pathology could not have failed to provide suggestions for lines of investigation in cancer research, had the general pathologist considered such fundamental facts as the immunity of the lens and cornea to cancer, the restriction of retinoblastoma to infancy, and the rarity of primary intraocular carcinomas. It happens, however, that recent trends in cancer research in England and the United States have thrown a flood of light on the basic etiology of the disease and it is now necessary for the ophthalmologists to examine the new facts and to apply them to the known clinical pathology of malignant disease of the eye, which can act largely as a touchstone. If the newer conceptions of the nature of cancer are found as applicable to the special case of the eye as to the general run of tumors then they will stand the test of time.

The vast amount of cancer research done throughout the world during the last 60 years has clarified the position and shown us the essential questions to be answered. We are faced with a disease having as its primary manifestation the continued unchecked multiplication of cells. We have been conversant with a host of apparent causes all of which are capable of initiating tumors (that is, starting cell division), but none of which can explain the continuance of the process long after the initial stimulus to growth has disappeared. We know that the initiating causes are multiple, both chemical and physical (for example, certain coal tar derivatives, such as 1:2 benzpyrene or methylcholanthrene; certain hormones, such as oestrin; certain radiations such as ultraviolet light, X rays, and radium emanations).

These are all known to "cause" cancer—that is to say, they start the cells dividing. But what is the "continuing cause," the mechanism which, once started, never runs down, though all traces of the initiating cause have disappeared?

For many years it was postulated that the action of the carcinogenic agent was similar to that of X rays on certain insects; that is, it produced a chromosomal mutation which then bred true. Since in the case of Drosophila it is the gametes which are affected, it is easy to prove a mutation since succeeding generations will show the variant. In the case of malignant change, however, it is a somatic cell which is affected so that mutation can never be proved.

Some support for the mutation theory was afforded both by the existence of cancer pedigrees in man and animals and by the familial incidence of certain tumors, particularly retinoblastoma. But, as we shall see later, a familial incidence does not necessarily imply a genetic defect, although at first sight the experiments in breeding of mice initiated by Leo Loeb, Maude Slye, and W. S. Murray before the first world war lend color to the theory that there may be an hereditary tendency toward such hypothecated somatic mutations.

These inbred strains of mice which were started in laboratories in the United States have since been continued in laboratories throughout the world and have seemed to demonstrate the hereditary nature of cancer

* From the Institute of Ophthalmology.

in the respect that strains exist (for example, the R3, C3H, and Strong-A strains) in which 70 to 95 percent of the females die of cancer of the breast, while in others (Simpson and the C57 black strain) few ever develop cancer. This fact taken alone might almost seem conclusive but it is capable of an entirely different explanation.

In 1911, the Rous chicken sarcoma was discovered and a complete re-orientation of our views became necessary. This tumor, which is clinically and histologically a spindle-celled sarcoma, is caused by a virus which, being intracellular, acts as the "continuing cause," stimulating the nucleus to divide and itself multiplying intracellularly indefinitely.

Since 1911, over 200 virus tumors of birds have been discovered, all of which can be transmitted by dried tumor tissue and by cell-free filtrates, thus proving the existence of a continuing cause which can survive the complete disintegration of the cell.

From its other properties also this intracellular cause is known to be a virus. It withstands drying, freezing to the temperature of liquid air, and storage in 40-percent glycerol, all of which kill avian and mammalian cells.

Inoculation with the virus produces tumors at the site of inoculation without the use of any of the usual carcinogenic agents. Since such tumors were only found in birds, a dichotomy of thought arose, mammalian tumors being considered to be somatic mutations arising in hereditarily predisposed animals from the action of carcinogenic agents and avian tumors being largely of virus origin, the virus itself possibly acting as the carcinogenic agent in a predisposed bird.

In 1937, however, Bittner, then at Bar Harbor and now of Minneapolis, Minnesota, demonstrated that the mammary cancers of the inbred strains of mice already referred to could be transmitted by a cell-free agent which could be isolated from the milk. This agent, now known to be a virus, exists in a latent form in the bodies of both male and female mice of the affected strains. The new-born mice acquire it from the mother when they suckle and it remains for a long period (the incubation period of other virus diseases) without producing tumors.

A chemical initiating cause, namely oestrin, activates it in the normal females in the course of 7 to 12 months, depending on the strain of mice, and they develop cancer of the breast. The males do not normally develop cancer but can be made to do so by the administration of oestrin. Mice of the cancer-free C57 black and Simpson strains do not contain the Bittner virus in their bodies but they can be infected with it by suckling them on infected mothers of other strains. Normally virus-free male Simpson or C57 mice cannot be made to develop cancer of the breast by painting with oestrin but they can be made to do so if infected with the Bittner virus in infancy. Conversely both male and female mice of a high cancer line can be rendered cancer free by cross suckling on Simpson mothers.

We therefore see that the pathology of adenocarcinoma of the mouse breast is that of a virus disease with a long latent period, the virus being eventually activated by a hormone. Until recently only the latent form in the milk could be transferred to noninfected stock and no tumors appeared until the mouse reached "the cancer age."

Now, however, workers at the Imperial Cancer Research Fund Laboratory, London,* have succeeded in obtaining the Bittner virus in its active form direct from the tumors, have dried it to free it from living cells, and have produced tumors with it in both male and female mice within a week or two of inoculation.

The virus is very thermolabile and the cells must be killed by freezing and drying done in vacuo at a temperature of $-10°C$. or lower. The virus so isolated is unstable and is tissue specific. No tumors are obtained unless it is injected into mammary tissue.

* Mann, I.: Brit. M. J., July 30, 1949.

Since it is in the active form, no carcinogenic initiator is required—hence the infectibility of male mice without oestrin.

We therefore see that the "cause" of mammary cancer in mice is the Bittner virus, that the apparent hereditary nature of the disease is due to inbreeding of the virus within the affected strains, and that the apparent complexity of the pathology resolves itself into the parasitization of a cell with a latent tissue-specific virus in infancy, later capable of being activated by a number of agents and in the active form stimulating the cell to divide without killing it.

This can be paralleled by the story of the herpes simplex virus. This is now known to enter the body in its latent form very early in life, to become parasitic in certain epithelial cells in a latent form, and to be capable of changing to the active form under certain conditions (usually a febrile reaction) and producing the clinical disease, herpes febrilis. This may be repeated at intervals in the case of herpes since the active form of the virus destroys the cells in which it lives and so the disease is self-limiting. In the case of the carcinoma virus the disease is incurable since the active form of the virus merely stimulates the cells to divide and multiplies with them till the tumor kills the host.

The carcinoma picture is therefore fairly clear. Does the same pathology also apply to the sarcomas? Professor Gye and his team at the Imperial Cancer Research Fund have shown that it does and that sarcomas can be started afresh by tumor tissue frozen and dried in vacuo as in the case of the carcinomas.

Since tissue from both spontaneous sarcomas and chemically induced tumors can be used in this way it appears obvious that in the former case the "initiating agent" was not known and in the latter it was a chemical deliberately applied. In both cases the active form of the sarcoma virus has been obtained free from living cells and has been made to initiate tumors afresh.

Viruses are well known to mutate with great ease and frequency and the large number of different tumors can be looked on as being caused by mutations of a cancer virus which have adapted themselves to become parasitic in different cells.

In the case of the Bittner virus the inbred strains of mice such as RIII carry only the mammary mutant; in the case of the C57 black strain the connective-tissue mutant is present only. These mice do not get spontaneous mammary cancer, nor can tumors be induced with oestrin, nor do they often get sporadic sarcoma (hence the deduction that the connective-tissue mutant is not activated by oestrin), but they can be made to develop sarcoma with great ease by injecting them with certain coal-tar derivatives.

These facts are not sufficiently appreciated by clinicians and it is interesting to try to relate them to tumors of the eye.

In the first place it is obvious that the cancer viruses must be carried by the blood stream, and that they may enter the body at or just after birth.* Hence we should expect only organs with a blood supply to be affected.

Secondly, it is probable that a cancer virus cannot stimulate a cell to divide unless that cell still has the power of mitosis. Cells so highly differentiated that they can no longer divide are not able to react to the stimulus of the virus.

Thirdly, the various virus mutants will remain latent in the individual and in their cells of election until they change to the active form. It is unlikely that infection can occur after infancy. This is borne out by the known facts concerning the herpes febrilis virus.

Fourthly, the number of experimental carcinogens known is legion and some of them have a chemical resemblance to substances occurring in the course of normal metabolism so that the fact that an "initiating cause" is not always obvious in man does not prove that human tumors are "causeless"

* There is some evidence that entry may be occasionally before birth.

as was once taught, even by such able pathologists as the pioneers of cancer research.

Fifthly, no experimental evidence exists of any genetic tendency to cancer, though the early passage of virus from mother to offspring produces an appearance of inheritability. This "handing on" is, however, of the virus and is not genetic.

With these points in mind we can begin to consider the eye. The first clinical fact which strikes us is the absence of malignant disease of the lens and of the cornea proper, and the extreme rarity of sarcoma of the sclera.

We know that the cells of the subcapsular epithelium of the lens undergo mitoses throughout life, that the fibroblasts of the sclera can proliferate to heal an injury, and that the cellular content of the substantia propria is capable of flux and the cornea of repair under various conditions.

The absence of malignant disease in these parts is therefore not due to their inert and fully differentiated condition, nor necessarily to the difficulty of any "activating" cause reaching them. Such causes are mainly chemical and could easily reach the tissues by osmosis and so forth.

The physical causes such as ultraviolet light, heat, and other radiations are obviously more than likely to affect the cornea and lens and yet they never induce malignant change.

We are attracted to the conclusion that the lens and cornea escape because no virus has ever reached the cells, on account of the absence of a blood supply. If this is not the cause of their immunity, then we must postulate some mysterious protecting mechanism.

In the case of the lens, it has been shown experimentally that this does not exist since the cells of the subcapsular epithelium are quite capable of giving rise to an epithelioma when they are given a blood supply containing latent virus and a chemical activator.* Lenses of new-born mice have been rendered malignant by this means, but it is obvious that the acquisition of a blood supply in later life (for example, through trauma, in man) will hardly be sufficient, since an epithelial mutant of the virus might not be present in the blood and the chemical or physical activator might be absent. Very few virus mutants capable of living in lens cells are likely to exist and might also be destroyed by the reaction which has produced vascularization of an injured lens.

The mechanism of escape of the cornea is also bound up with its lack of blood supply, and the almost universal localization of epibulbar epitheliomas to the limbal region where the blood supply is greatest bears this out. There is no essential difference between limbal and corneal epithelial cells nor between the amount of trauma to which they are each subjected. The obvious difference is in their blood supply in early life.

The sclera has a poor blood supply and is almost entirely immune to malignant change. When this occurs, it is seen most often at the insertion of one or other of the extrinsic muscles where the blood supply is better than in the intervening regions and where the growth may have started in the muscle. These facts strongly support the view that the cancer viruses reach the affected organs via the blood stream in early life.

We have now to consider what parts of the eye would be expected to be immune to cancer on account of their state of complete differentiation. The retina (pars optica) has differentiated by the end of the sixth month of life and none of its cells are capable of dividing again, except occasionally a few astrocytes in the glial supporting tissue.

What is more, practically all the differentiation occurs before a blood supply is developed at all. Indeed the spread of the blood vessels is from the disc toward the periphery as is the differentiation also, this latter preceding the vascularization by many weeks throughout development. The only situation where development lags behind is the fovea centralis and this is devoid of blood vessels throughout life.

* Mann, I.: Induction of an experimental tumor of the lens. Brit. J. Cancer, 1:63, 1948.

Malignant tumors of the retina would therefore be expected to be rare (as they are) on account of the fact that differentiation is practically complete before a blood supply appears. They would also be expected to appear very early in life or even before birth (as they do) since only then could the cells involved divide.

The retinal mutant of the virus may be conveyed through the placenta. It may be that in the affected cases differentiation had lagged behind vascularization slightly. The placental passage of virus would account for the familial incidence; the only genetic possibility is that of an inherited lag in differentiation which would allow the blood supply to reach undifferentiated cells. With the story of the Bittner milk virus in our minds we must be chary of postulating genetic influence in familial neoplasms.

True astrocytomas of the retina are excessively rare and may arise at any age. Tumors of the hexagonal epithelium are unknown and this differentiates very early. Malignant growths, carcinomas, of the ciliary body occur but are rare. One, the diktyoma, arises early in infancy or before birth. The true ciliary epithelioma, however, occurs in adults and this is not surprising when we remember that the ciliary epithelium can hypertrophy in case of injury or inflammation and is thus capable of division throughout life.

The common malignant melanoma of the choroid presents no difficulties as it arises in all probability from the ectodermal Schwann cells lying in the extremely vascular choroid. Cases of apparent inheritance of malignant melanoma are known. One family, reported by Davenport, shows the passage for three generations through affected females, the offspring of unaffected individuals being normal. This will fit equally well into a genetic pattern or into the picture of a virus mutant conveyed from mother to child. Tumors of the iris and choroid are also as simple of explanation as connective-tissue tumors elsewhere.

We thus see that both the study of cancer and of ophthalmology have something to gain by collaboration. The tumor incidence in the vascular and avascular, differentiated and undifferentiated regions of the eye affords support for the virus origin of malignancy. The study of the mode of transmission of the Bittner virus in mice affords an explanation of the apparent familial and hereditary forms of cancer in ophthalmology.

Certain problems cry out for solution still, before all is clear. Are there other portals of entry for the virus than the transplacental and mammary routes? How late in life can entry of the virus occur? Can the virus ever be carried as a "passenger" by the sperm?* What are the activators which in man convert the latent virus to its active form? We can produce a host of such queries but, in spite of this, the newer knowledge on cancer causation accords more nearly with the facts of ocular pathology than did previous theories.

Finally, the narrowing of the field of investigation which recent researches have brought about brings us hope for the future. There are obviously three points at which we can seek to attack the disease, namely, before it enters the body, while it is still latent, and after it has changed into its active form and become manifest. Although this is a formidable problem it is less awe-inspiring than the search for the prophylaxis of a mutation occurring unpredictably, or its cure by its reversal.

* "Passenger viruses" are well known in animals.

FLICKER FUSION FIELDS*

II. Technique and Interpretation

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The critical point at which a flickering light of decreasing frequency is first perceived to flicker is a phenomenon which lends itself well to clinical use in testing the perception of small areas of retina. Unlike all other tests, flicker fusion frequency depends on (1) the length of the latent period between the light stimulus and the beginning of the response, and (2) the ability of cones (or groups of light-adapted elements including cones) and their pathways to recover from the inhibitory period following one stimulus and become receptive to another.

Injured retinal elements may transmit correct impressions of brightness intensity and form vision involved in the usual tests of visual field and acuity, and be defective in flicker fusion frequency.

Electronic instruments have been used for study of flicker fusion fields since 1938,[1] and the technique is now so simple and satisfactory that it should be put to use. Its advantages are many.

Flicker fusion fields are less affected than ordinary fields by poor visual acuity, refractive blur, peripheral aberrations and low peripheral acuity, translucent defects of the ocular medias, suppression amblyopia,[2] reduced intelligence and attention. Contrary to previous reports, flicker fusion frequency is not necessarily reduced by old age and small pupils.[3]

The eye is more sensitive to flicker fusion frequency in the periphery (10° to 30°) than centrally, and flicker fusion frequency is therefore more likely to detect defects from diseases which affect the peripheral field first.

Flicker fusion frequency is a number so that gradations of perception are measured automatically without time-consuming use of various sized and colored discs. Time required for taking fields is reduced.

Tachistoscopic tests differ from flicker fusion frequency in that perception of objects exposed for brief intervals can improve with training, particularly in peripheral retina. Flicker fusion frequency is not altered either by training or fatigue. Tyler,[4] in 1947, reported tests on 600 subjects who remained awake from 30 to 60 hours without change in flicker fusion frequency.

Lythgoe and Tansley[5] (1939) found day-to-day variation of flicker fusion frequency to be 2.9 percent in the worst subject; 0.6 percent in the best. Brozek and Keys[6] (1944) found readings in 56 normal adults to vary less than one percent from day to day. Curves on the variation of flicker fusion frequency with intensity, area, light-dark phase, distance from fovea, and so forth, are parallel in all normal individuals.

Phillips[7] (1933) made the first study of flicker fields on patients. Although he restricted his tests to 17 areas of the visual field, his targets were adequate and his controls good. He found that 2.5 (cm.) targets gave a central flicker fusion frequency of 43 flashes per second, with gradual decrease toward the periphery, while similar 3.5 targets gave a central flicker fusion frequency of 49, with increase in 10-degree peripheral intervals to 56, 50, 44, and 41. He found a decrease in flicker fusion frequency in eight chiasmal and two parietal brain tumors. The two parietal cases had normal visual acuity and fields.

Granit and Harper[8] (1930), Creed and Ruch[9] (1932), and others had also found that targets larger than 1.5 degrees are necessary

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to get the increased flicker fusion frequency peripherally over central. Small targets eliminate the effect of summation or interaction of nerve pathways in the periphery, but reduce the flicker fusion frequency to a low value not useful clinically. Increasing the target intensity has much less effect in peripheral retina than increasing the area.

The same authorities demonstrated the important fact that flicker fusion frequency

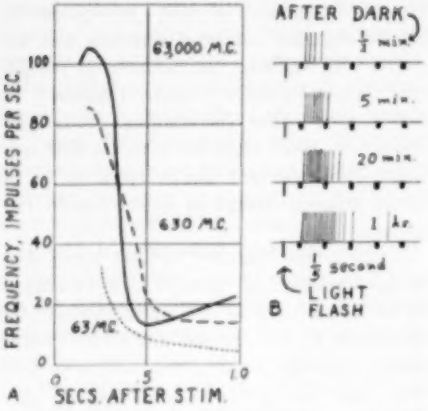

Fig. 1 (Miles). (A) Frequency of wave train from one flash stimulus, eye of Limulus. (B) Effect of dark adaptation on the same wave train. (A and B redrawn from Hartline.[11])

drops markedly with one hour's dark adaptation, so that central readings become as low as 12 flashes per second, with decrease peripherally, regardless of target area. Small pupils reduce the retinal illumination and therefore the flicker fusion frequency but, after two hours of miosis, adaptation is such that the readings return to a normal level.[3] Small pupils cannot result in dark adaptation in the usual sense, because light cannot be reduced more than 24 fold, and the eye is sensitive to a total range 100,000 fold. Perhaps cone vision adapts to the reduced illumination.

Among other evidences that flicker fusion frequency is a phenomenon of cone vision, is the study of Hecht[10] (1948) on the flicker fusion frequency of totally color-blind patients. Such eyes are supposedly cone-free, and have a central scotoma. He reported a reduction of flicker fusion frequency from a normal of 55, with his test conditions, to about 20.

Information somewhat related to flicker fusion frequency was presented by Hartline[11] (1932, 1940) (fig. 1). He showed that the electrical response in the optic nerve of Limulus followed the all or none law in regard to amplitude but that, from one flash of light, not one wave but a train of waves resulted, lasting about 0.3 seconds (A, fig. 1). The frequency of this wave train depended on the stimulus intensity (metercandles in A, fig. 1), the state of dark adaptation of the specimen (B, fig. 1), and the wave length (color) of the stimulus. One intense flash might set up a train of impulses 100 per second, while a flash just above threshold would elicit 36 per second. With increasing dark adaptation, the wave train had increasing frequency.

Data on higher animals show a simultaneous negative electrical response in the nerve fiber following a flash of light. This negative response is increased more than the positive phase by higher flash intensities. Therefore, the positive discharge is more quickly neutralized by higher flash intensities, the response is shorter in duration, and the inhibition period (assumed equal to the wave pattern length) is shortened, permitting higher flicker fusion frequency. Higher stimulus intensity raises flicker fusion frequency also, by shortening the latent period between the flash and the onset of the response.

Crozier[12] (1937) by ingenious experiments tested the flicker fusion frequency in many species of the lower animals and compared it to the human with similar conditions. All data were "essentially homologous."

Early experiments[5,6,9] showed that, regardless of target intensity and size, there is a marked drop in flicker fusion frequency

when the background surrounding the flickering target is completely dark. This phenomenon is important in illumination for such activities as reading or observing television, and was first described by Cobb[13] in 1916. There should be moderate general illumination of the periphery for the best local perception. Cobb[14] stated that the sensitivity to flicker is highest when the test field is set in surroundings of about its own brightness, and that sensitivity decreases markedly with a brighter surrounding. Decrease in sensitivity is more moderate with a darker surrounding. He also agreed with Crozier that flicker fusion frequency sensitivity was greater with shorter intervals of light in the light-dark cycle.

This justifies my clinical practice of testing flicker fusion frequency in patients adapted to ordinary waiting-room illumination, and not reducing the illumination greatly during the tests.

Crozier[12] believed that a more reliable end point in testing vision by flicker fusion frequency could be obtained by varying the intensity instead of the flicker rate. This would complicate the procedure, but might prove a useful advance.

It is still unknown why individuals vary so greatly in the flicker fusion frequency rate. Gelson and Guilford[15] (1933) found that people with little pigment in the iris and retina have higher absolute light thresholds than those more densely pigmented. This is not true of flicker fusion frequency.

If flicker fusion frequency stimulates primarily the cones, the target might properly be red. Willmer[16] (1946) found that to identify the color of a light flashed briefly in the light-adapted eye, the least duration of flash was required with orange. Longer time was required with violet, blue, and yellow. In an eye dark adapted for one hour, the least duration of flash required was still with orange. Mandelbaum[17] (1941) reported that light thresholds to red are the same in different parts of the retina notwithstanding the variation of the cone population. Cogan and Cogan[18] (1938) found that colors steadily observed by peripheral retina tend to desaturate and appear gray. This so-called fatigue is least with the color red in the light-adapted eye. Field defects in lesions of the nerve-fiber layer, optic nerve, tract, and brain are usually more typical by use of red targets in ordinary field techniques. It is therefore reasonable to suppose that in tests for flicker fusion frequency a target light with an excess of red or orange should be satisfactory.

Phillips[7] was not the only one to take flicker fields. Niederhoff[19] (1936, 1941) devised and use a mechanical flickering target in a perimeter.

Riddell[20] (1936) reported flicker fields on 58 patients, concluding, "the flicker method is to have a place in ophthalmic work." In patient J. O. H., he showed a total hemianopia by flicker fusion frequency where the ordinary field showed only a temporal slant. He believed one should not expose one retinal area more than three seconds to flicker, because fatigue might eliminate the flicker sensation. This is prevented by starting the flicker rate well above the flicker fusion frequency, and having the patient say "now" the instant flicker is certain as the rate is gradually decreased.

Mayer and Sherman[1] (1938) reported on normals using a neon tube target, 1 to 3 degrees in diameter, at a distance of 25 cm. on a perimeter.

Werner[21] (1942) tested 20 children with brain injury, and found a decreased flicker fusion frequency. Enzer[22] (1942) found in 45 normals central flicker fusion frequency of 45, while 13 hypothyroid patients had 36.3 (33 to 41); in four patients treated with methyl testosterone it changed from 43 to 46.6; benzedrine increased it three flashes per second.

Hylkema[23] (1942) used a mechanical flicker device and confirmed the effect on fields of intensity, target size, dark adapta-

tion, and background illumination. He found the highest possible flicker fusion frequency was 82 flashes per second between 200 and 800 candles per sq. M. Figure 2-A shows Hylkema's normal field using a medium intensity target 0.4 cm.

Weekers[24] (1946, 1947, 1948) reported

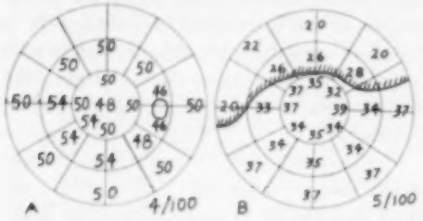

Fig. 2 (Miles). (A) Normal flicker fusion field obtained by Hylkema.[20] (B) Flicker fusion field showing defect due to detached retina. (Weekers,[24] 1948.)

clinical studies of such conditions as nicotinic neuritis, glaucoma, compression of optic pathways, and detached retina (fig. 2-B). He used an improved sector disc method in which the target was mobile about a red fixation light. He tested 26 different areas of the 30-degree visual field, with targets from 3 to 7 degrees, at a distance of 100 cm.

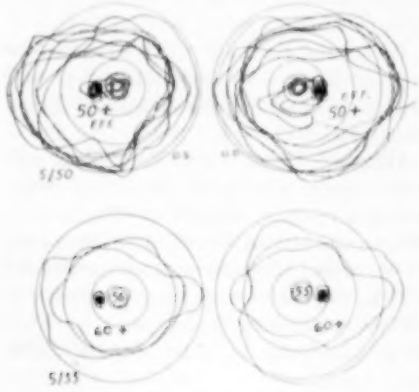

Fig. 3 (Miles). Superimposed drawings of flicker fields in normal eyes, taken on a perimeter with the target light fixed in position, five cm. diameter, 50 cm. from the eye (33 below).

Present methods

The flicker target was a five-cm. disc of fine white paper on which was focussed the light of a gas-discharge tube. This red-orange light could be turned completely on and completely off for intervals of 0.00001 seconds at frequencies between 10 and 64 per second to be read from a dial. At high

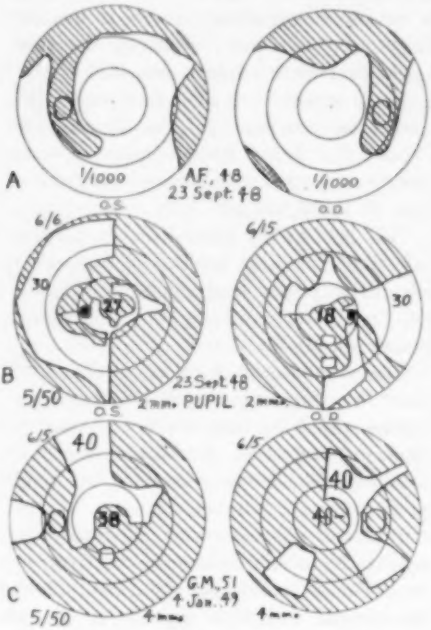

Fig. 4 (Miles). Flicker fusion frequency fields in glaucoma, first technique. (A) Central fields above. (B) Normal central and peripheral fields taken by the usual method.

speed, it deflected a photo-electric meter in direct contact without shield six foot-candles. The target was placed in the center of a 50-cm. perimeter. In the second method, the target was concentrated so that the light measured 10 foot-candles, and was placed on the end of a wand. By this means a standard one-meter tangent screen could be used, and flicker fusion frequency determined for any point out to 30 degrees.

The patient was placed to look monocular-

ly at the center of the target disc and was shown that the light could appear steady or flickering. Then the rate was gradually reduced from a fused level until the patient said "now" as flicker first became apparent. This was repeated until it become constant, showing that the patient understood the test. For the perimeter test, the rate was fixed about five cycles per second faster (usually 50) than that found centrally, and the patient turned the eye and to some extent the head to fix a movable target held by the examiner.

As the eye turned from 90 degrees centrally, the patient reported "flicker" and "stop" and the area of perception of flicker was plotted. Figure 3 shows normal fields obtained in this way. Central flicker fusion frequency was about 42, and an annular area of higher flicker perception extended approximately to the limits of normal peripheral fields. Twenty patients were tested by this method. The fields showed abnormal flicker, but field contours did not conform well to those by the usual technique.

Figure 4-A and B shows fields in two

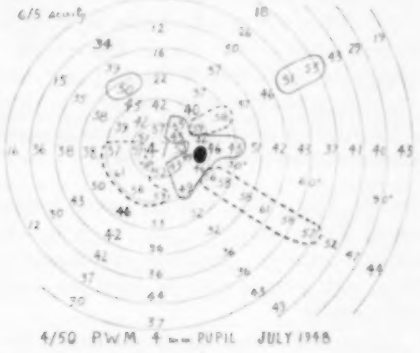

Fig. 5 (Miles). Normal flicker field on perimeter, highest inferior nasal and temporal.

cases of glaucoma. A. F., aged 48 years, had a complaint of pain and blurring for several months. Vision 6/15, and 6/6. Although the tension was: O.D., 30 mm. Hg; O.S., 27 mm. Hg (Schiøtz), the gonioscope showed narrow angles and several peripheral anterior synechias, and there was disc cupping, especially on the right. Ordinary fields were normal peripherally, but showed (A) typical central scotomas. Flicker fields (B) were de-

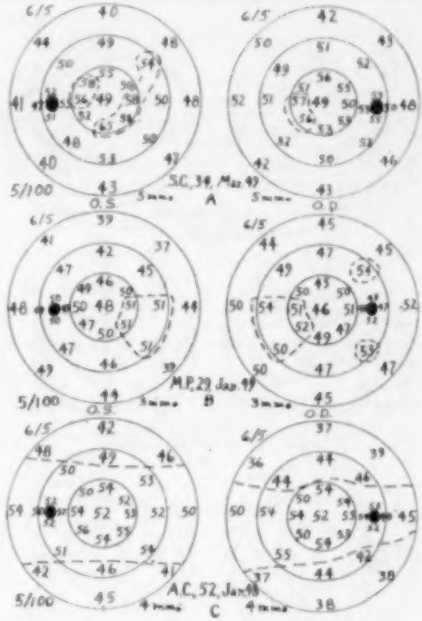

Fig. 6 (Miles). Flicker fusion fields in three normal subjects.

pressed generally 15 to 20 per second, and there were large sector and arcuate defects. Iridectomy was performed bilaterally with improvement.

Figure 4-C shows the flicker fields of G. M., aged 51 years, a glaucoma suspect. Her acuity and ordinary fields were normal, but she had complaint of pain and blurring, there was increased cupping of the discs, and the pupils were large. Tension was only 21 mm. Hg (Schiøtz) but it increased to 27 mm. Hg with the lability pressor test, O.S. Later tests showed tension to be 23 mm. Hg and 25 mm. Hg under pilocarpine miosis. The flicker fusion frequency fields were slightly depressed peripherally, and there was baring of the blindspot.

Figure 5 shows the flicker fusion frequency field of a normal eye taken on a perimeter to show that, if the target is kept at a constant distance from the eye, the flicker fusion frequency does not drop off as

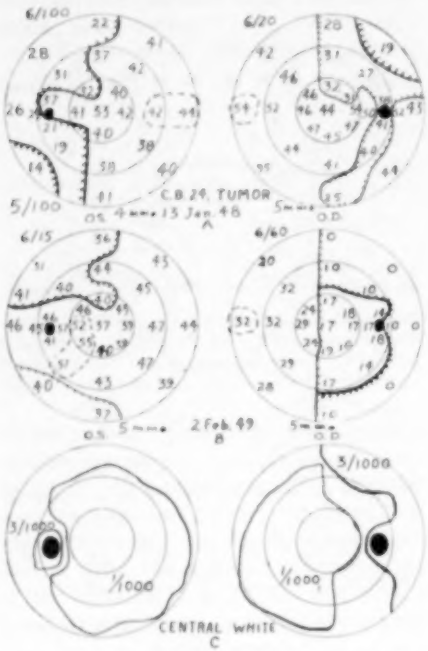

Fig. 7 (Miles). Flicker fields before and after removal of tumor from optic nerve of the right eye at the chiasm.

abruptly in the periphery as it does in tests on the tangent screen.

Figure 6 shows flicker fusion frequency fields taken on the tangent screen with the second technique. The readings were taken and recorded on paper forms. If any reading was considered abnormal or suspect, it was repeated. (A) is the field of a graduate student, (B) is that of a housewife with depressive psychosis, and (C) is that of a colored man, aged 52 years.

Figure 7 shows the flicker fusion frequency fields on C. B., aged 24 years, the day before operation for a tumor attached to the sheath of the right optic nerve at the chiasm. At this time (A), the visual acuity was: O.D., 6/20, O.S., 6/100, worse in the left eye. Central and peripheral fields were difficult to take, but showed slight questionable temporal loss bilateral.

Flicker fusion frequency fields showed (A) general overall depression, especially on

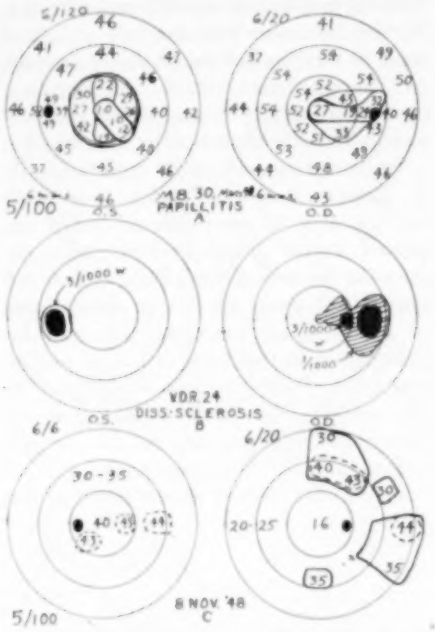

Fig. 8 (Miles). Flicker fields to illustrate central scotoma and normal periphery compared to central scotoma (C) with depressed periphery.

the left. There was marked temporal hemianopia, fairly complete on the left, and marked superior temporal quadrantopia, right, with extension of the blindspot down and medially.

Figure 7-B shows the flicker fusion frequency fields 19 days after surgery, while (C) shows the central field changes at the same time. Vision had improved, L.E., to 6/15; regressed, R.E., to 6/60. Ordinary fields showed definite temporal loss, O.S., and O.D., but not as great as flicker fusion frequency loss (B). The entire right field was depressed, with an absolute hemianopia in the lateral 30-degree area, and partial from 0 to 20 degrees. An area of normal

flicker fusion frequency appeared, left inferior temporal field.

Figure 8-A shows flicker fusion frequency fields of M. B., aged 35 years, which were taken a week after the onset of bilateral papillitis of unknown origin. Ordinary fields were unsatisfactory due to poor fixation in each eye. The left eye had an absolute central scotoma about 10 degrees in diameter, but the right relative scotoma could not be outlined at all by ordinary methods. Flicker fusion frequency fields showed (A) on the left a central scotoma of three gradations of density. The patient's finger tip was placed in the center of the field during the tests. Note in contrast with (C) that the periphery is normal.

Figure 8-B represents the central field of a patient with known early disseminated sclerosis, with a well-defined centrocecal scotoma, right eye. Figure 8-C shows flicker fusion frequency fields taken by the first technique. Although the ordinary fields are normal in the left eye, there is general flicker fusion frequency depression over the whole field. It is almost extinguished centrally on the right and the periphery is depressed.

Figure 9-A shows the ordinary central fields and (B) the flicker fusion frequency fields of a patient who had had a pituitary adenoma removed seven months before. (A) shows an indefinite temporal slant, left eye, and a distinct temporal partial hemianopia, right eye; (B) shows superior temporal defects bilateral, left eye, almost complete, right eye, absolute, with definite relative complete bilateral temporal hemianopia. There is general flicker fusion frequency depression, enlargement of the blindspot of the right eye, and field loss in the right superior nasal area.

Figure 9-C shows flicker fusion frequency fields of I. L. B., aged 29 years, with right papillitis of unknown etiology. Although the visual acuity was reduced, no definite edges to the scotomatous area could be detected by ordinary field technique. The flicker fusion frequency field of the right eye shows marked general depression, more peripheral than central, with a temporal defect which includes the blindspot. There is even more depression in the nasal superior and middle region. The peripheral defect and the fact that she improved makes one suspect disseminated sclerosis.

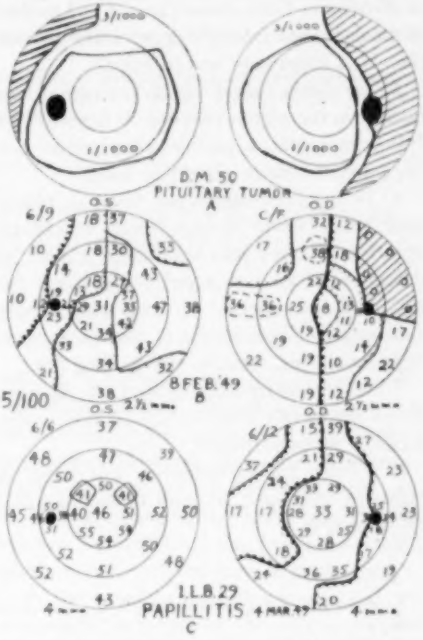

Fig. 9 (Miles). To illustrate the adjacent-column technique in fields with suspected hemianopia.

It is evident that flicker fusion frequency fields show more definite changes in the diseases illustrated than do ordinary fields. It is, of course, possible that special measures like reducing the illumination or using various sized and colored targets at increased distances might have improved the "ordinary" fields.

Interpretation of Flicker Fusion Frequency Fields

More cases have been studied which will be reported later. Undoubtedly, refinements of the technique will be developed. At present, however, the criteria for flicker fusion frequency field interpretation are:

1. Central flicker fusion frequency should

be 42 or more, the periphery generally 5 or more higher out to the 20-degree tangent, and then no less than central flicker fusion frequency out to 40 degrees.

2. The highest flicker fusion frequency is usually found in the inferior nasal field 10 to 20 degrees from center; lateral and medial is much higher from 30 degrees and on out than it is superiorly and inferiorly.

3. To obtain reasonable flicker fusion frequency in the region between 30 degrees and 100 degrees out, a perimeter technique, not the tangent screen, should be used.

4. If any area except the fovea or blindspot has a lower flicker fusion frequency than the adjacent peripheral area, it must be defective. If an area appears depressed, the test should be repeated. In fields where quadrantanopia or hemianopia is suspected, readings should just straddle the dividing line.

5. If the periphery beyond 20 degrees drops uniformly low, it may be due to age changes or small pupils.

6. Flicker fusion frequency will detect an enlarged blindspot, so tests should be made all around it.

7. There may be five flashes per second difference in the normal two eyes centrally, but the periphery should be almost identical. Comparison is particularly useful in diseases which begin unilaterally such as glaucoma. Central differences are due to the same conditions which make flicker fusion frequency in amblyopia ex anopsia equal centrally and peripherally.

Summary and Conclusions

The advantages of flicker fusion frequency as a test of perception of the whole visual field are discussed. Some physical and physiologic facts on flicker fusion frequency bearing on possible techniques are reviewed. Experiences of seven other clinicians with flicker fusion frequency fields are cited.

The results of testing flicker fields by two methods in normal controls and in some types of diseases are illustrated.

An improved, but certainly not perfected, technique is described, and criteria for interpretation made in detail.

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References

1. Mayer, L. L., and Sherman, I. C.: A method of flicker perimetry. Am. J. Ophth., **21**:390 (Apr.) 1938.
2. Miles, P. W.: Flicker fusion frequency in amblyopia ex anopsia. Am. J. Ophth., **32**:225 (June, Part II) 1949.
3. ———: Flicker fusion fields: I. The effect of age and pupil size: Am. J. Ophth., **33**:769 (May) 1950.
4. Tyler, D. B.: The fatigue of prolonged wakefulness. Federation Proc., **6**:218 (Mar.) 1947.
5. Lythgoe, R. J., and Tansley, K.: The adaptation of the eye: Its relation to the critical fusion frequency. London, Spec. Report Ser. Med. Res. Council, No. 134, 1929.
6. Brozek, J., and Keys, A.: J. Indust. Hyg. & Toxicol., **26**:169 (May) 1944.
7. Phillips, G.: Perception of flicker in lesions of the visual pathways. Brain, **56**:464-478, 1933.
8. Granit, R., and Harper, P.: Am. J. Physiol., **95**:211, 1930.
9. Creed, R. S., and Ruch, T. C.: Regional variations in sensitivity to flicker, J. Physiol., **74**:407-423, 1932.
10. Hecht, S., et al.: Complete color blindness, J. Gen. Physiol., **31**:459-472, 1948.
11. Hartline, H. K., and Graham, C. H.: Nerve impulses from single receptors in the eye of Limulus. Proc. Soc. Exper. Biol. & Med., **29**:613-615, 1932; J. Optic. Soc. America, **30**:239-247, 1940.
12. Crozier, W. J., Wolf, E., and Zerrahn-Wolf, G.: J. Gen. Physiol., **21**:203-247, 1937-8.
13. Cobb, P. W.: The effect on foveal vision of bright surroundings. J. Exper. Psychol., **6**:540, 1916.
14. Cobb, P. W.: The dependence of flicker on the dark light ratio of the stimulus cycle. J. Optic. Soc. America, **24**:107, 1934.
15. Gelson, H., and Guilford, J. P.: The relation of visual sensitivity to the amount of retinal pigment, J. Gen. Psychol., **9**:58-76, 1933.
16. Willmer, E. N.: Retinal Structure and Color Vision. London, Cambridge Univ. Press, 1946, p. 151.
17. Mandelbaum, J., and Mintz, E. U.: The sensitivity of the color receptors as measured by dark adaptation. Am. J. Ophth., **24**:1241, 1941.

18. Cogan, D. G., and Cogan, F. C.: Color fatigue in the retinal periphery. Ophthalmologica, **96**: 136-153, 1938.

19. Niederhoff, P.: Das flimmer-perimeter, ein apparat zur genauen Untersuchung des gesichtsfeldes. Klin. Monatsbl. f. Augenh., **96**:601 (May) 1936; **107**:257-265 (Sept.) 1941.

20. Riddell, L. A.: The use of the flicker phenomenon in the investigation of the field of vision. Brit. J. Ophth., **20**:385-410 (July) 1936.

21. Werner, H.: Critical fusion frequency in children with brain injury. Am. J. Psychol., **45**:394, 1942.

22. Enzer, N., Simonson, E., et al.: J. Lab. & Clin. Med., **29**:63 (Jan.) 1944; Ann. Int. Med., **16**:701, 1942.

23. Hylkema, B. S.: Examination of visual fields by determining fusion frequency. Acta Ophth., **20**: 159-193, 1942.

24. Weekers, R., and Roussel, F.: Measurement and clinical importance of apparent persistence of visual sense, Bull. d. Soc. Belg. d'Opht., **83**:27-36, 1946; Bull. Soc. Franc. d'opht., **60**:331-337, 1947; Ophthalmologica, **110**:242, 1945; **112**:305, 1946; **115**:297, 1948.

THE THRESHOLD GRADIENTS OF THE RODS AND THE CONES: IN THE DARK-ADAPTED AND IN THE PARTIALLY LIGHT-ADAPTED EYE*

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INTRODUCTION

A study of the variation in retinal sensitivity to light from center to periphery is of theoretical interest for comparison with known anatomic and physiologic factors which might be expected to play a part in determining retinal sensitivity.

The two principal factors considered in this study are the variation in effective area of pupil, and the variation in density of the retinal receptors. Knowledge of the retinal sensitivity gradient of the normal eye is also of value in interpreting the results of certain clinical tests of ocular function. The purpose of the standard perimetric test is to examine the entire visual field from center to periphery for evidence of subnormal function.

The functions usually tested are brightness and color sensitivity. If ability to perceive chromatic color is mediated solely by the cones, then perimetric examination with colored targets tests the integrity of the cone but not of the rod mechanism. When a white test object is used, the extent of the visual field depends upon the gradient of brightness sensitivity. Whether the cone mechanism alone is tested, or whether both rods and cones are involved, is determined by the relative sensitivity of the two mechanisms, which varies with the state of adaptation.

In the completely dark-adapted eye the achromatic threshold of the rods is well below that of the cones. If, therefore, the visual field were examined with a white test object of low brightness, when the eye is fully dark adapted, the extent of the field would depend upon the sensitivity of the rods.

In perimetry as ordinarily practiced, however, the eye is not adapted to darkness. In the Ferree-Rand perimeter, for example, the gray arc has a brightness of about 0.7 ml. At the limit of the visual field for a given white test object where it is just above the threshold, whether the test object is perceived by cones, by rods, or by both depends upon their relative sensitivities at this level of adaptation. To devise adequate tests which distinguish between cone and rod function, and to interpret the result of standard peri-

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metric examinations, data are needed on the variation in sensitivity, from center to periphery, of the cones and of the rods, determined under various experimental conditions.

Experimental procedure

In the present study, the method used to isolate cone and rod thresholds in each retinal region was to measure the decrease in thresholds during adaptation to darkness or to a low brightness level after previous adaptation of the eye to a high brightness. In a retinal region containing both types of receptor the adaptation curve shows two distinct sections, the first of which is generally considered to be determined by the cones, the second by the rods.

The instrument used to adapt the eye to a high brightness level, and to measure the subsequent course of dark adaptation in any desired region of the retina, has been described in previous articles.[1] The procedure used in the present study was as follows:

The eye was exposed for a period of three minutes to an evenly illuminated field whose brightness was 1,100 ml. The visual angle covered by the preëxposure field was approximately 62 degrees in the horizontal dimension, 53 degrees in the vertical. In each case the direction of fixation during the period of light adaptation was such that the preëxposure surface was centered approximately at the point in the visual field at which the adaptation curve was to be determined.

At the completion of the period of light adaptation, the illumination of the preëxposure field was turned off, and a determination of the light threshold of the selected retinal region was made immediately. Additional measurements were taken at intervals until the subject had been in darkness for 40 or more minutes, or until there was no further significant decrease in the threshold.

Essentially the same method was used to measure the course of adaptation to a lower brightness instead of to complete darkness. In this case the illuminated arc of the perimeter on which the threshold tester was mounted provided the lower brightness level to which the eye adapted.

After a period of three minutes of adaptation to 1,100 ml., the region of the retina studied was constantly exposed to this lower brightness, except during the short intervals in which the subject looked at the fixation target while threshold measurements were made. The test field consisted of a completely dark circular area, 2.5 degrees in diameter, at the center of which the one-degree test spot was flashed on for periods of one second until a threshold measurement was obtained.

Adaptation curves were measured at a series of 20 locations in the horizontal meridian, including the fovea and extending to 50 degrees from the fovea in the nasal field, 90 degrees from the fovea in the temporal field. Determinations were made of the course of adaptation to complete darkness, and to a brightness of 0.7 ml. The latter was chosen because it corresponds to the level of adaptation of the eye in the clinical tests made with the Ferree-Rand perimeter. In addition, adaptation curves at 15 degrees in the nasal field were made under other experimental conditions designed to influence the relative sensitivities of cones and rods.

Results

Part I. Determination of cone and rod thresholds of dark-adapted eye

Figures 1 to 3 show the adaptation curves for the different retinal locations when the eye adapts to complete darkness. Each curve is based on data obtained in a single test. Retests at 15, 20, and 30 degrees in the nasal field gave final threshold which agreed within 0.1 log unit. It may be seen that, with the exception of the adaptation curve of the fovea, all consist of two distinct sections. In some locations, namely at 20 degrees nasal, 30 and 50 degrees temporal, at the time of the sudden break in the curve the cone thresholds had not reached a constant value and were still decreasing slightly. In such cases the final cone threshold was estimated

by extrapolation of the curve to determine the intensity at which the plateau would occur.

Column 2 of Table 1 gives, for each retinal location, the final cone threshold of the dark-adapted eye. The variation in this threshold from center to periphery is shown graphically in Curve B of Figure 4. Column

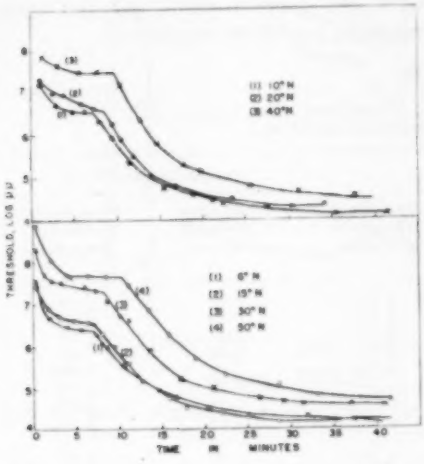

Fig. 1 (Sloan). Rate of adaptation to darkness after pre-adaptation to 1,100 ml. The location in the visual field at which each adaptation curve was determined is indicated on the graph.

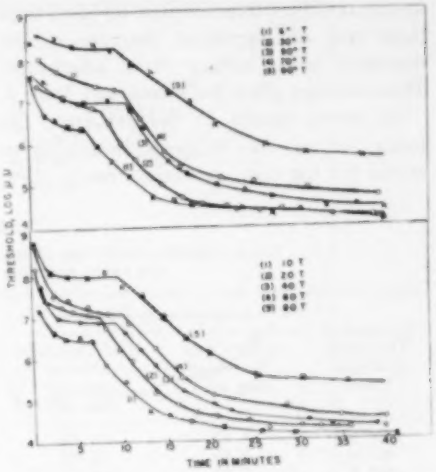

Fig. 2 (Sloan). Rate of adaptation to darkness after pre-adaptation to 1,100 ml. The location in the visual field at which each adaptation curve was determined is indicated on the graph.

3 of Table 1 gives the rod thresholds after 40 minutes of dark adaptation.

Inspection of the curves shows that in some instances the thresholds at this time had not reached a constant level but were still decreasing slightly. In order, therefore, to obtain measurements of the thresholds of the fully dark-adapted eye, additional determinations were made. In these tests, meas-

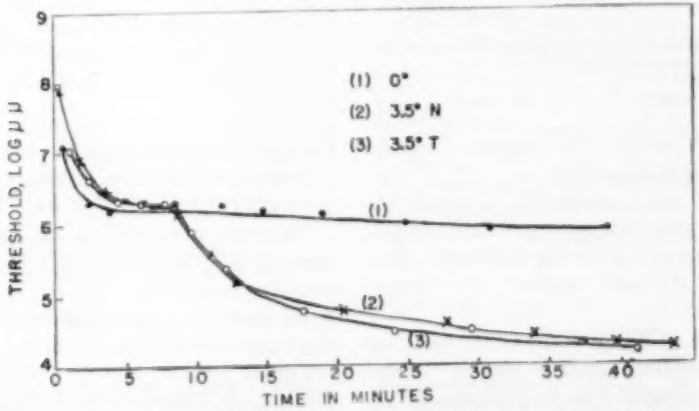

Fig. 3 (Sloan). Rate of adaptation to darkness after pre-adaptation to 1,100 ml. The location in the visual field at which each adaptation curve was determined is indicated on the graph.

urements at each location were repeated until there was no significant decrease in the threshold with further dark adaptation. These data are given in Column 4 of Table 1.

At points within 15 degrees from the fovea the two sets of measurements agree within 0.1 log unit, indicating that in these regions 40 minutes was adequate to insure complete dark adaptation.

In the more peripheral locations, the threshold after 40 minutes of dark adaptation is from 0.2 to 0.5 log unit higher than the final threshold reached after longer adaptation.

Curve A of Figure 4 shows the variation in threshold from center to periphery of the fully dark-adapted rods for comparison with the corresponding threshold gradient of the cones. The cone gradient shows a minimum at the fovea and rises gradually toward the periphery. The rod thresholds are high in the paracentral regions near the fovea, decrease to a minimum in the midperiphery of the nasal and temporal fields, and rise again gradually toward the periphery.

TABLE 1

LIGHT THRESHOLDS OF THE CONES AND OF THE RODS WHEN ADAPTED TO DARKNESS AND TO A BRIGHTNESS OF 0.7 ML

Location of Test Spot in Visual Field	Adaptation to Darkness		Adaptation to 0.7 ml.		
	Final Cone Threshold (log μl.)	Rod Threshold after 40 minutes (log μl.)	Final Rod* Threshold (log μl.)	Final Cone Threshold† (log μl.)	Final Rod Threshold† (log μl.)
50° N‡	7.67	4.70	4.46	7.90	7.61
40° N	7.50	4.48	4.23	7.88	7.47
30° N	7.10	4.57	4.14	7.74	7.26
20° N	6.52	4.19	4.09	7.48	7.09
15° N	6.50	4.12	4.05	7.36	6.99
10° N	6.55	4.10	4.13	7.22	6.96
6° N	6.40	4.17	4.25	7.15	6.79
3.5° N	6.10	4.30	4.30	6.85	6.68
0° N	5.90	—	—	6.72	—
3.5° T§	6.35	4.35	4.35	6.90	6.71
6° T	6.30	4.15	4.14	7.15	6.84
10° T	6.40	4.10	4.05	7.20	6.89
20° T	6.95	4.30	4.00	7.45	6.97
30° T	6.70	4.23	4.05	7.30	7.01
40° T	6.80	4.31	4.11	7.45	7.09
50° T	6.93	4.40	4.08	7.80	7.39
60° T	7.00	4.51	4.29	7.97	7.63
70° T	7.20	4.70	4.35	8.16	7.92
80° T	7.90	5.30	4.80	8.54	8.34
90° T	8.18	5.58	5.13	8.80	8.66
Retests					
15° N	6.55, 6.50	4.20			
20° N	6.62, 6.55	4.19, 4.29			
30° N	7.20	4.55			

* Average results of tests on two different days.
† Results of one to four tests.
‡ N = Nasal.
§ T = Temporal.

PART II. DETERMINATION OF CONE AND ROD THRESHOLDS OF THE PARTIALLY LIGHT-ADAPTED EYE

The rate of decrease in threshold while adapting to a brightness of 0.7 ml., after previous adaptation to 1,100 ml., was studied in the same 20 retinal locations. A typical adaptation curve for each location is shown in Figures 5 and 6.

While the difference in level in the two plateaus of the adaptation curve is much less

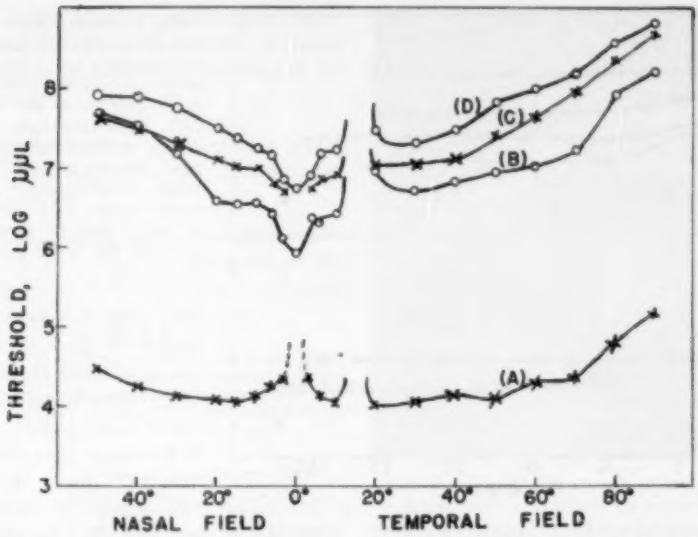

Fig. 4 (Sloan). Retinal threshold gradients for the horizontal meridian. (A) Rods: dark adaptation. (B) Cones: dark adaptation. (C) Rods: adaptation to 0.7 ml. (D) Cones: adaptation to 0.7 ml.

marked than when the eye adapts to darkness, a definite break in the curve is present for all retinal locations except the fovea. If we assume that the slight break in these curves is likewise caused by a transition from pure cone to pure rod response, as before we may determine from each curve the threshold of the cones and of the rods when the eye is adapted to a brightness of 0.7 ml.

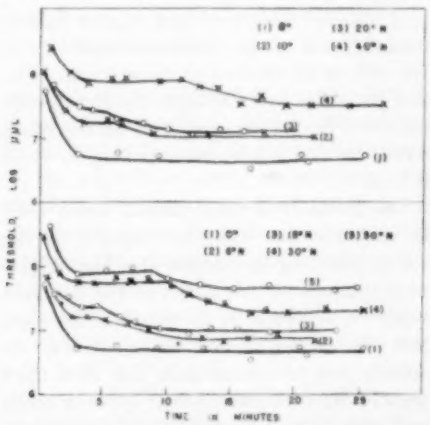

Fig. 5 (Sloan). Rate of adaptation to 0.7 ml. after pre-adaptation to 1,100 ml. The location in the visual field at which each curve was determined is indicated on the graph.

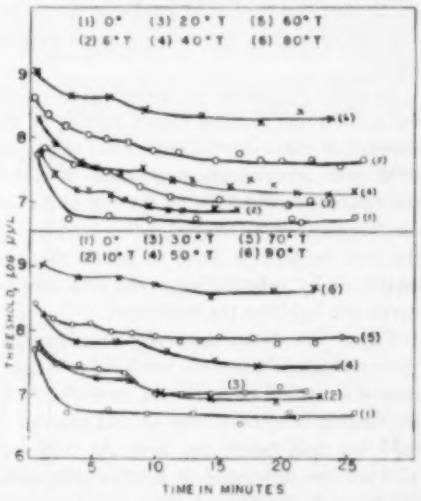

Fig. 6 (Sloan). Rate of adaptation to 0.7 ml. after pre-adaptation to 1,100 ml. The location in the visual field at which each curve was determined is indicated on the graph.

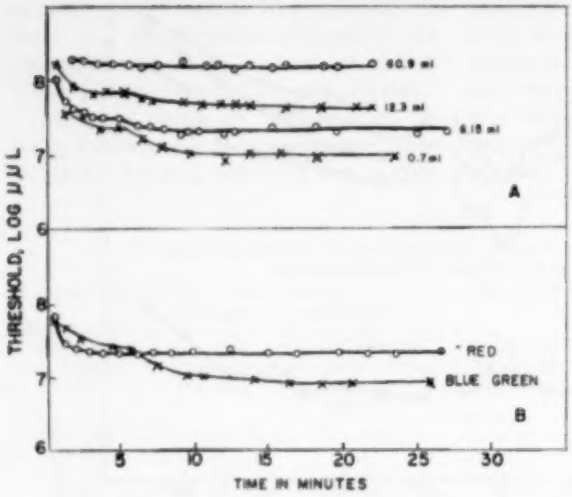

Fig. 7 (Sloan). Rate of adaptation to a lower brightness after pre-adaptation to 1,100 ml. The adaptation curves were measured at 15 degrees in the nasal field. (A) White test light. Effect of change in the brightness level to which the eye adapts. The brightnesses in millilamberts are shown on the graph. (B) Adaptation to 0.7 ml. Effect of change in the color of the test light.

The threshold gradients are shown graphically in Curves D and C of Figure 4. The rod-threshold gradient of the partially light-adapted eye differs significantly in shape from that of the fully dark-adapted eye, and in fact runs almost parallel to the cone gradient. This difference in contour is unexpected if the two rod-threshold gradients are actually determined by the same receptor mechanism.

In order, therefore, to investigate further the assumption that the second section of the adaptation curve depends upon rod response, additional experiments were made in which the relative sensitivities of the rod and cone mechanisms were changed, either by varying the low brightness level to which the eye adapts or by substituting a red or a bluish-green test light for the white one.

Figure 7A shows the series of adaptation curves obtained when the level of low brightness was varied from 0.7 ml. to 60.9 ml. At the lowest brightness the second plateau is 0.35 log unit below the first. At 6.15 and 12.3 ml. the difference in level is only about 0.2 log unit. At 60.9 ml. there is no evidence of a second section in the adaptation curve.

These findings are compatible with the view that the latter represents rod thresholds, since with increase in the brightness level to which the eye is adapted the rod sensitivity might be expected to decrease more rapidly than that of the cones. If at some brightness level above 12.3 ml., the rod sensitivity becomes less than that of the cones, then the entire curve should depend upon cone response.

Figure 7B shows the adaptation curves for a red and for a bluish-green test light. (These were provided by Wratten filters, Nos. 25 and 65A.) With green light the curve shows two definite plateaus; with red light, only one. These findings are also to be expected if the second section of the curve depends upon rod response.

It does not appear when a red test light is used, because of the relative insensitivity of the rods in this region of the spectrum. For this particular red test light, the rod threshold must be greater than that of the cones when the eye is adapted to a brightness of 0.7 ml.

On the basis of these data, it seems valid to conclude that the two sections of the curves showing adaptation to a low brightness measure the thresholds of two different types of receptor. It is possible, however, that the second section represents the response, not of typical rods, but of a third type of receptor intermediate between cones and rods. This possibility is supported by some of Granit's electrophysiological studies which led him to conclude[2] that there must be a second type of rod reacting like cones

insofar as adaptation is concerned and probably containing a modified form of visual purple capable of mediating responses in the photopic state.

Part III. Correction of threshold measurements for decrease in effective area of pupil

One of the factors which must play an important role in raising the threshold of the peripheral retina is the decrease in effective area of the pupil with increased distance from the pupillary axis. If measurements are made of the decrease in apparent diameter of the pupil from center to periphery, it is possible to apply a correction factor to the thresholds, so that these may be expressed in terms of the amounts of light actually reaching the retina.

In order to obtain data on the variation in effective diameter of the pupil of the subject used in this study, a series of photographs were taken at various angles of eccentricity. The equipment used is described in a previous paper.[3] A typical photograph is illustrated in Figure 8, showing the appearance of the subject's pupil when viewed from a point 90 degrees to the temporal side of the point of fixation.

TABLE 2

Decrease in effective diameter of pupil with distance from axis of fixation: Correction factors for each location to compensate for reduction in amount of light reaching the retina

Distance from Axis of Fixation	Ratio of Horizontal to Vertical Diameter of Pupil	Correction Factor (log units*)
10° N	0.98	−0.01
0°	1.00	0.00
10° T	0.998	−0.01
20° T	0.946	−0.02
30° T	0.905	−0.04
40° T	0.851	−0.07
50° T	0.756	−0.12
60° T	0.629	−0.19
70° T	0.505	−0.28
75° T	0.488	—
80° T	0.414	−0.41
90° T	0.242	−0.62
92° T	0.210	—
96° T	0.175	−0.76

* Computed from data read from smoothed curve.

Fig. 8 (Sloan). Photograph of pupil at 90 degrees from visual axis in the temporal field.

Table 2 and Figure 9 give the ratios of horizontal to vertical diameter for locations from 10 degrees in the nasal field to 96 degrees in the temporal field. These ratios, rather than the horizontal diameters themselves, were used in computing the correction for effective area, in order to allow for slight differences in actual size of pupil on the different days on which the photographs were taken.*

* There are two reasons why the effective di-

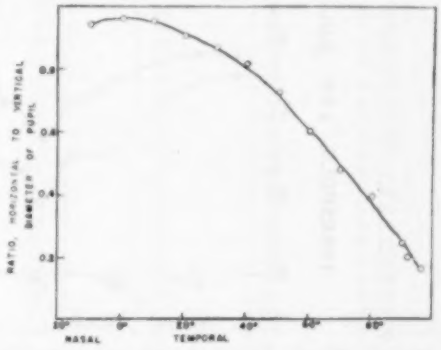

Fig. 9 (Sloan). Decrease in apparent horizontal diameter of pupil with distance from the visual axis.

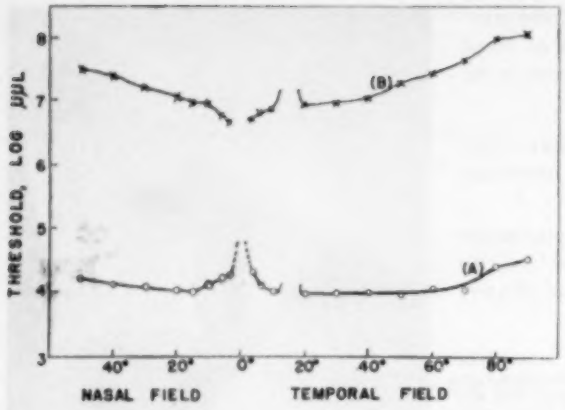

Fig. 10 (Sloan). Threshold gradients of rods after correction for decrease in effective area of pupil. (A) Dark adaptation. (B) Adaptation to 0.7 ml.

The correction factors in logarithmic units are given in Column 3, Table 2. It may be seen that the correction is less than 0.1 log unit for locations within 40 degrees from the fixation point, but is of significant magnitude in the far periphery. Figures 10 and 11 show the rod and cone threshold gradients after correction for effective size of pupil. The corrected thresholds are given in Columns 2 to 5 of Table 3.

PART IV. RELATIONSHIPS BETWEEN THRESHOLD GRADIENTS AND DENSITY GRADIENTS OF RETINAL RECEPTORS

In order to compare the threshold gradients with the variation in density from center to periphery of the retinal receptors Osterberg's data, quoted by Ten Doesschate,[5] have been used. Figure 12 shows in logarithmic units the density per sq. mm. of the rods and of the cones.

Inspection of these curves and those for the light thresholds indicates that only the gradient of the fully dark-adapted rods, when corrected for decrease in effective size of pupil, closely resembles the density gradient of the rods. In the case of the partially light-adapted rods, there is no rise in threshold in regions near the fovea corresponding to the decrease in rod density in this area.

Neither of the two threshold gradients of the cones agrees closely with the density

ameter of the pupil does not decrease to zero at 90 degrees from the visual axis.[4] The most important factor operating to permit light to reach the retina from objects 90 degrees or more from the visual axis is the effect of corneal refraction on the apparent diameter of the pupil. Since the pupillary axis of most subjects is about five degrees temporal to the visual axis, there may be a further extension of the possible limit of the temporal field.

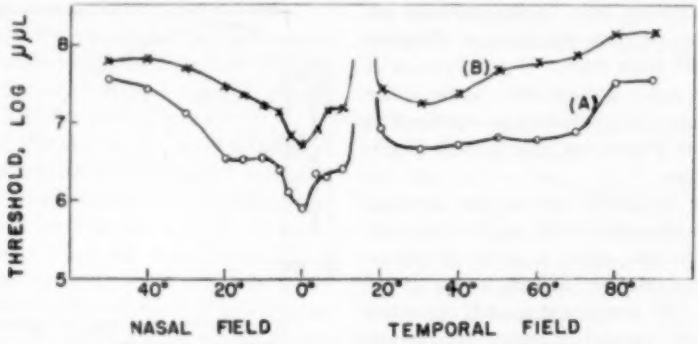

Fig. 11 (Sloan). Threshold gradients of cones after correction for decrease in effective area of pupil. (A) Dark adaptation. (B) Adaptation to 0.7 ml.

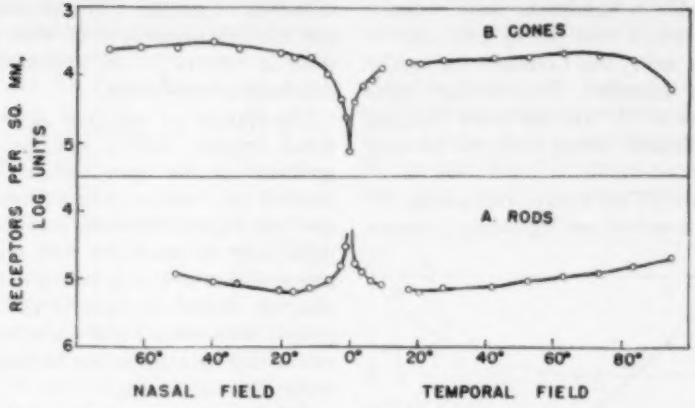

Fig. 12 (Sloan). Variation in areal density of rods (A) and cones (B) from center to periphery. (From Ten Doesschate's data[6] based on Osterberg's studies.)

gradient of these receptors. The decrease in cone density from fovea to paracentral areas is much more rapid than the increase in threshold. In the midperiphery cone density remains relatively constant but the threshold shows a gradual rise. In the far periphery there is an increase in cone density but no corresponding decrease in cone threshold.

The close relationship between rod thresholds of the fully dark-adapted retina and the areal density of the rods is shown in Table 4 and Figure 10. Column 2 of the table gives

TABLE 3

THE LIGHT THRESHOLDS OF THE CONES AND OF THE RODS AFTER CORRECTION FOR DECREASE IN THE EFFECTIVE AREA OF THE PUPIL

Location	Light Threshold: Adaptation to 0.7 ml.		Light Threshold: Adaptation to Darkness	
	Cones (log μμl.)	Rods (log μμl.)	Cones (log μμl.)	Rods (log μμl.)
50° N	7.78	7.49	7.55	4.24
40° N	7.81	7.40	7.43	4.16
30° N	7.70	7.22	7.11	4.10
20° N	7.46	7.07	6.54	4.07
15° N	7.35	6.98	6.51	4.04
10° N	7.22	6.96	6.55	4.13
6° N	7.15	6.79	6.40	4.25
3.5 T	6.85	6.68	6.10	4.30
0°	6.72	—	5.90	—
3.5 T	6.90	6.71	6.35	4.35
6° T	7.15	6.84	6.30	4.14
10° T	7.20	6.89	6.40	4.05
20° T	7.43	6.95	6.93	3.98
30° T	7.26	6.97	6.66	4.01
40° T	7.38	7.02	6.73	4.04
50° T	7.68	7.27	6.81	3.96
60° T	7.77	7.43	6.80	4.09
70° T	7.86	7.62	6.90	4.05
80° T	8.16	7.96	7.52	4.42
90° T	8.18	8.04	7.56	4.51

TABLE 4

DATA SHOWING THAT THE LIGHT THRESHOLD OF THE DARK-ADAPTED RODS VARIES INVERSELY AS THEIR AREAL DENSITY

Location	Log Threshold (μμl.) of Dark-Adapted Rods	Log Density (rods per sq. mm.)	Sum of Columns 3 and 4
50° N	4.24	4.94	9.18
40° N	4.16	5.02	9.18
30° N	4.10	5.10	9.20
20° N	4.07	5.15	9.22
15° N	4.04	5.16	9.20
10° N	4.13	5.12	9.25
6° N	4.25	5.02	9.27
3.5° N	4.30	4.88	9.18
3.5° T	4.35	4.88	9.23
6° T	4.14	4.98	9.12
10° T	4.05	5.09	9.14
20° T	3.98	5.15	9.13
30° T	4.01	5.15	9.16
40° T	4.04	5.11	9.15
50° T	3.96	5.05	9.01
60° T	4.09	5.00	9.09
70° T	4.05	4.94	8.98
80° T	4.42	4.85	9.27
90° T	4.51	4.75	9.26
		Average	9.17±0.06

the thresholds in logarithmic units; Column 3 the number of rods per sq. mm., also in logarithmic units; and Column 4 the sum of these two quantities. The average value of this sum is 9.17 and the mean variation of the individual values from the average, ±0.06.

In Figure 13 the inverse relationship between log threshold and log density is shown

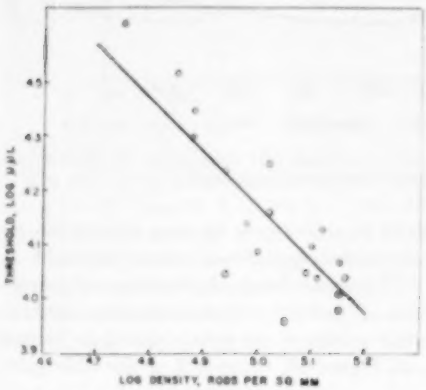

Fig. 13 (Sloan). Relationship between the values of light threshold of the dark-adapted rods and the corresponding values of receptor density.

graphically. The equation of the straight line is log T + log D = 9.17.* It will be noted that the deviation of the actual values of log T from those required by the equation is 0.1 log unit or less in 17 of the 19 measurements. This is as close agreement as could be expected in view of the fact that repeated determinations of the threshold may vary by 0.1 log unit in the more central regions of the retina and by greater amounts in the far periphery.

In the fully dark-adapted eye, therefore, the variation in rod threshold from center to periphery may be attributed almost entirely to the changes in effective size of pupil and in number of receptors. If other factors play any role, the magnitude of their effects is small in relation to the reproducibility of threshold measurements.

The absence of any close agreement between receptor density and the threshold gradients of the cones and of the light-adapted rods remains to be explained. Lythgoe[6] has suggested that the process of adaptation may be associated with synaptic rearrangements such that, during dark adaptation, the retinal elements in effect acquire progressively more nerve fibers in common, and during light adaptation become progressively more segregated.

It is known that there is greater summation among rods than among cones, and if the amount of rod summation increases with decrease in the level of adaptation, as Lythgoe suggests, it is to be expected that the thresholds of the fully dark-adapted eye in different retinal regions might show a simple inverse relationship to the areal density of the rods. At somewhat higher levels of adaptation, where summation plays a less important role, this simple relationship would no longer hold for the rods.

If there is likewise much less summation of impulses from individual cone than rod receptors, then the variation in cone threshold from center to periphery may be expected to depend primarily on factors other than variation in cone density. What these factors might be, we are not prepared to say.

The hypothesis of three rather than two different types of receptor offers a possible explanation for the observed fact that only the dark-adapted rods show a close relationship between light sensitivity and receptor density.

In Osterberg's investigation, two types of receptor were differentiated, except in the foveal region, on the basis of a difference in diameter. If we assume that this criterion gives correct figures for the density gradient of typical rods which function in the dark-adapted eye, but does not distinguish between cones and modified rods which func-

* In arithmetic units the equation may be written as T times D equals 1.48, in which T equals the threshold in micromillilamberts and D is the number of rods per square micron.

tion in light adaptation, then close agreement between receptor density and light sensitivity would be expected only in the case of the rod thresholds of the dark-adapted eye.

Part V. Applications of findings to perimetric studies

The findings of this study are of practical interest in relation to clinical perimetry, since they provide information as to the relative importance of rod and cone response in determining the extent of the field for a white test object, in the partially light-adapted eye. The conclusions reached do not depend upon acceptance or rejection of the hypothesis presented in the previous section that light-adapted and dark-adapted rods are independent retinal receptors.

When the visual field is examined with the Ferree-Rand perimeter, the eye is adapted to a brightness of about 0.7 ml. The present study has shown that at this level of adaptation, in the normal eye the threshold of the light-adapted rods for a one-degree stimulus is slightly below that of the cones. The extent of the normal visual field for a white test object depends, therefore, upon the sensitivity of these rods.

Complete loss of function of the cones, associated with normally functioning light-adapted rods, should therefore not cause any decrease in the size of the field. With intact cones and loss of function of the light-adapted rods, either with or without a corresponding defect in the dark-adapted rods, there should be only a slight contraction of the field. This is because the limits are now determined by the response of the slightly less sensitive cones. A significant contraction of the field, demonstrable with a one-degree white test object, should occur only if there is impairment of both the cones and the light-adapted rods.

If this conclusion is correct, the success of clinical perimetric examination with white test objects probably depends upon the fact that most types of ocular pathology result in impairment of function of both cones and rods. Conditions known to affect only one type of retinal receptor are in fact relatively rare.

Although vitamin-A deficiency causes primarily an increase in threshold of the dark-adapted rods, there is experimental evidence that the light-adapted rods and the cones may also show slight impairment of function.

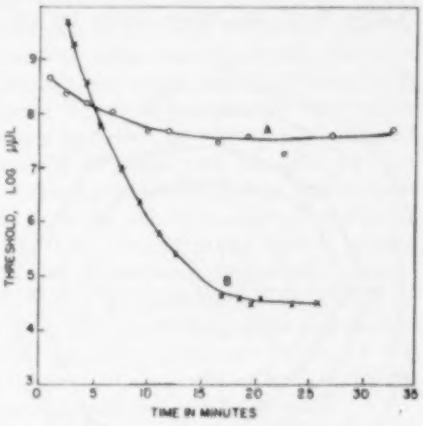

Fig. 14 (Sloan). Rate of adaptation to darkness after pre-adaptation to 1,100 ml. (A) Patient with congenital night blindness. (B) Patient with congenital achromatopsia.

Hecht and Mandelbaum[7] found a slight increase in the cone threshold of some subjects following an experimentally produced vitamin-A deficiency. I have found[8] that some patients with a marked deficiency show moderate contraction of the visual field for a white test object. Fields of normal extent were found in other cases of vitamin-A deficiency. On the basis of the findings of the present study, contraction of the visual field may be interpreted as evidence of involvement of both the cones and the light-adapted rods.

Congenital night blindness and congenital achromatopsia are generally attributed to loss of function of the rod and of the cone mechanisms, respectively. I have examined one case in which a probable diagnosis of congenital night blindness could be made, and

several cases of typical congenital achromatopsia.*

The adaptation curve of the night-blind subject, with change from 1,100 ml. to darkness, is shown in Curve A of Figure 14. The lack of a second section in the curve indicates that even after long adaptation to darkness the rods, if they function at all, are less sensitive than the cones.

Curve B of this figure shows the corresponding dark-adaptation curve of a subject with typical congenital achromatopsia. This curve has only a rod section, indicating absence of or marked impairment of cone function. The visual fields of these two subjects were determined on a Ferree-Rand perimeter with a one-degree white test object. In both cases the fields were well within normal limits (fig. 15).

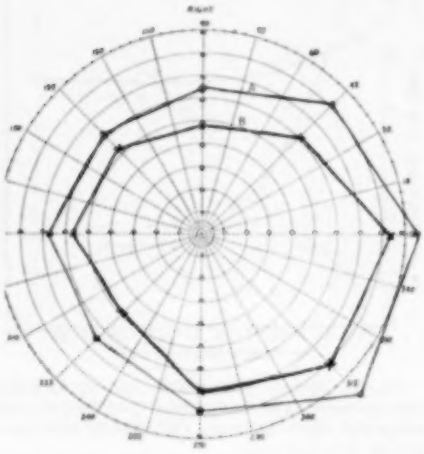

Fig. 15 (Sloan). Visual fields for a one-degree (6/330) white test object. (A) Patient with congenital night blindness. (B) Patient with congenital achromatopsia.

These findings and the normal fields observed in many cases of vitamin-A deficiency indicate that the relatively rare pathologic eye conditions affecting primarily only one retinal mechanism cannot be adequately studied by a routine perimetric examination with white test objects.

Isolated involvement of the cone mechanism is revealed by means of ordinary perimetric examination with red and blue test objects. Defects involving only the light-adapted rods, if such can occur, would probably be difficult to detect by any simple procedure. If only the dark-adapted rods are impaired or nonfunctioning, the defect can be detected by measurement of the threshold in the fully dark-adapted eye. Examination of the entire visual field by this method requires that the threshold gradients be determined in at least the horizontal, the vertical, and two oblique meridians.

A more rapid method of testing visual function in the dark-adapted eye consists in application of the techniques of ordinary perimetry, using a self-luminous fixation target and test objects whose brightnesses are below the cone threshold. Livingston[9] used this method to examine the central field of normal subjects and of patients with various eye diseases. Mann and Sharpley[10] employed the same technique to determine the outer limits of the normal scotopic field in different age-groups.

An adequate evaluation of the possibilities and limitations of scotopic perimetry requires further study. The most suitable sizes and brightnesses of the test targets must be determined and studies must be made with these targets to determine the range of variation in the fields of normal subjects.

Summary and Conclusions

Determinations were made for one subject of the variation in light threshold of the cones and of the rods in the horizontal meridian, when the eye was adapted to darkness and when it was adapted to a brightness of 0.7 ml. The decrease in effective diameter of this subject's pupil from center to periphery was determined by photography. From analysis of these data and Osterberg's figures on the density gradients of the cones and

* Detailed findings regarding these cases will be reported in later papers.

rods, the following conclusions may be drawn:

1. When correction is made for the decrease in effective area of the pupil from center to periphery, the rod threshold of the fully dark-adapted eye varies inversely as the areal density of the rod receptors.* The rod threshold of the light-adapted eye does not show this simple relationship to rod density. The cone threshold is not closely related to cone density, either in the dark-adapted or in the light-adapted eye.

2. The relationship between light threshold of the dark-adapted rods and their density suggests that summation of impulses from these receptors plays an important role in determining this threshold.

3. To explain the lack of agreement between receptor densities and threshold gradients of the cones and of the rods when light-adapted, it is suggested that light-adapted rods may actually be a third type of receptor, which, in Osterberg's study, was not distinguished from cones.

4. When the eye is adapted to a brightness corresponding to that employed in clinical studies of the visual field, the threshold of the light-adapted rods differs only slightly from that of the cones. Perimetric examination with white test objects will, therefore, probably not reveal defects affecting only one of the retinal mechanisms. This conclusion is confirmed by studies of two patients, one with congenital night blindness, the other with congenital achromatopsia. In both cases, the fields for white test objects were normal.

5. If the perimetric examination includes the use of chromatic test objects, isolated defects of the cone mechanism will be revealed. The examination must include scotopic perimetry with test objects of low brightness if isolated involvement of the dark-adapted rods is to be detected.

The Johns Hopkins Hospital (5).

* A study published after this paper was written (J. Ten Doesschate: Extra-foveal scotopic absolute threshold and the distribution of retinal rods. Ophthalmologica, **117**:110-115, 1949) reports similar findings as to the close relation between scotopic threshold and rod-density.

References

1a. Sloan, L. L.: An apparatus for studying regional differences in light sense. Arch. Ophth., **22**: 233-251, 1939.

1b. Jewett, H. J., Sloan, L. L., and Strong, G. A.: Does vitamin-A deficiency exist in clinical urolithiasis? J.A.M.A., **121**:566-568, 1943.

2. Granit, R.: Sensory Mechanisms of the Retina. London, Oxford Univ. Press, 1947, p. 253.

3. Sloan, L. L.: Size of pupil as a variable factor in the determination of the light minimum. Arch. Ophth., **24**:258-275 (Aug.) 1940.

4a. Stiles, W. S., and Crawford, B. H.: The effect of a glaring light source on extrafoveal vision. Proc. Roy. Soc. Med., **122**:255-280 (Series B) 1937.

4b. Spring, K. H., and Stiles, W. S.: Apparent shape and size of the pupil viewed obliquely. Brit. J. Ophth., **32**:347-352 (June) 1948.

5. Ten Doesschate: Visual acuity and distribution of percipient elements on the retina. Ophthalmologica, **112**:1-18 (July) 1946.

6. Lythgoe, R. J.: The mechanism of dark adaptation, a critical resume. Brit. J. Ophth., **24**:21-43, 1940.

7. Hecht, S., and Mandelbaum, J.: The relation between vitamin A and dark adaptation. J.A.M.A., **112**:1910-1916, 1939.

8. Sloan, L. L.: Rate of dark adaptation and regional threshold gradient of the dark-adapted eye. Am. J. Ophth., **30**:705-720 (June) 1947.

9. Livingston, P. C.: The form and character of rod scotometry. Am. J. Ophth., **27**:349-353, 428, 1944.

10. Mann, I., and Sharpley, F. W.: The normal visual (rod) field of the dark-adapted eye. J. Physiol., **106**:301-304, 1947.

THE OPTICS OF CYLINDER MAGNIFICATION*

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The linear magnification of objects by spherical lenses receives considerable and adequate coverage in most texts on ophthalmic optics. This is quite justifiable in view of the many instances in physiologic and practical optics where the size of the retinal image has to be considered. The tacit assumption is made that the dioptric system of the eye acts like a spherical lens and is, therefore, subject to the same basic laws as for that type of lens.

It is well known, however, that a good number of human eyes are astigmatic and that the astigmatism in the majority of these eyes stems from variations in the curvature of the cornea. The dioptric systems of such eyes are not spherical but rather spherocylindrical in character.

It may, therefore, be of some importance to consider linear magnification by cylindrical lenses, how it differs from spherical lenses, and its effect on the size of retinal images. Strangely enough most standard texts on ophthalmic optics deal with this subject by completely disregarding it, probably as part of their effort to simplify optics for nonmathematically inclined minds. The proofs are, however, relatively easy to demonstrate.

First, by way of review, it is well to recall that the image produced by a spherical lens depends upon the formula: $O/I = f/f'$, where O = object size, I = image size, f = object distance from lens, and f′ = image distance from lens (fig. 1).

Another useful formula is:

$$O/I = \tau/F,$$

where F = the anterior principal focal distance of the lens and τ = the distance from object to anterior principal focus (fig. 1).

Notice that in each instance the image size varies directly as the size of the object. The position of the image is determined in meters by the well-known formula:

$$1/f + 1/f' = 1/F,$$

or by the more easily handled vergence formula:

$$V + D = V',$$

where V is the dioptric distance between object and lens, D is the dioptric strength of

$$\frac{O}{I} = \frac{f}{f'} \quad \text{or} \quad \frac{O}{I} = \frac{\tau}{F}$$

Object and image position

$$\frac{1}{f} + \frac{1}{f'} = \frac{1}{F} \quad \text{or} \quad V + D = V'$$

Example

$V = -2$, $D = +6$

$-2 + 6 = V' = +4 = 25$ cm.

$$I = \frac{Of'}{f} = \frac{4 \times 25}{50} = 2 \text{ cm.}$$

Fig. 1 (Hallett). Linear magnification by spheres.

the lens and V′ is the dioptric distance between lens and image (fig. 1). With the latter formula all divergent rays are given the minus sign and all convergent rays the plus sign.

To apply these formulas consider the following example (fig. 1), which can easily be set up and measured on an optical bench: Describe the image produced by an illuminated vertical slit, 4 cm. long, situated 50 cm. (2D.) away from a +6D. spherical lens.

Substituting in the vergence formula:

$$V = -2, D = +6,$$

$V' = V + D = -2 + 6 = +4D. = 25$cm. Thus, a vertical linear image will be formed

* Read at the first annual Wills Hospital Conference, Philadelphia, May, 1949.

at 25 cm. on the other side of the lens. The image size:

$$I = Of'/f = 4 \times 25/50 = 2 \text{ cm.}$$

Now, study the familiar Figure 2 which shows the production of a line focus, bc, parallel to the vertically placed axis, XX′, of a convex plano-cylinder by an object point, O.

Considering only the axial rays, OX′b and

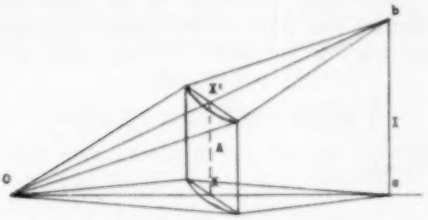


Fig. 2 (Hallett). Linear magnification by plano-cylinders.

OXc, the geometric form of Figure 3 is obtained. Let bc = I, the image, XX′ = A, the aperture, OX = f, the distance from object to lens, and Xc = f′, the distance from lens to image.

From the properties of similar right angle triangles the following formula for linear magnification by plano-cylinders is derived:

$$I/A = f + f'/f.$$

Note that, unlike spherical lenses, the image size varies directly as the aperture of the lens and bears no relationship to the size of the object. In other words, to emphasize a well-known fact, a point or a line object produce the same size image. The distances f and f′, which set the relative positions of the image, lens and object, are determined in accordance with the same vergence formula as for spherical lenses.

An example, which again can easily be set up and checked on the optical bench, may help demonstrate the application of the magnification formula. Describe the image produced by a point source of illumination 33 cm. away from a +8D. cyl. ax. 90° with an aperture of 3 cm. (fig. 4). Substituting in the vergence formula, V = −3, D = +8, V′ = −3 + 8 = +5D. = 20 cm. Thus, a vertical line image will be formed 20 cm. on

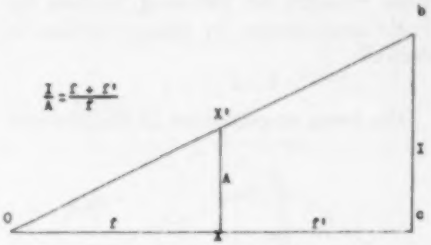


Fig. 3 (Hallett). Linear magnification by plano-cylinders.

the other side of the lens. The image size:

$$I = A\ (f + f')/f = 3\ (33 + 20)/33 = 4.8 \text{ cm.}$$

Referring back to Figure 3, it is evident that the axial rays, OX′b and OXc, continue in straight undeviated lines because they pass through a plane of the cylinder having zero dioptric power. In a sphero-cylinder axis 90°, however, such a condition does not exist; there is some strength in the axial

$$\frac{I}{A} = \frac{f+f'}{f}$$

Example—

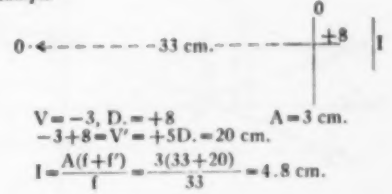


Fig. 4 (Hallett). Linear magnification by plano-cylinders.

plane and, consequently, the axial rays are deviated or refracted, along with the rays passing through the infinite number of vertical planes parallel to the axial plane, to meet at and form perpendicularly to the plane of this sheet the horizontal posterior line focus, Ip (fig. 5).

Let the distance between the anterior line

focus, Ia, and Ip = s, the interval of Sturm, and the distance from the lens to Ip = t. Again from the properties of similar right angle triangles the following formula for linear magnification by sphero-cylinders is derived:

$$Ia/A = s/t.$$

The linear magnification of the posterior

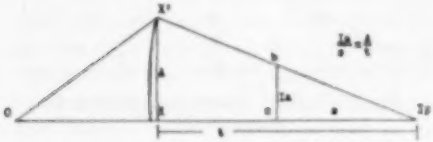


Fig. 5 (Hallett). Linear magnification by sphero-cylinders.

line focus, Ip, depends upon the same relationship. This is most conveniently demonstrated by assigning a higher dioptric power to the vertical axial plane of the above figures than to the horizontal plane.

Now (fig. 6), the axial rays meet at and cross to form the horizontally disposed Ia perpendicular to the plane of this sheet before forming the vertical Ip in the plane of this sheet. Let t now represent the distance from the lens to Ia and, again from

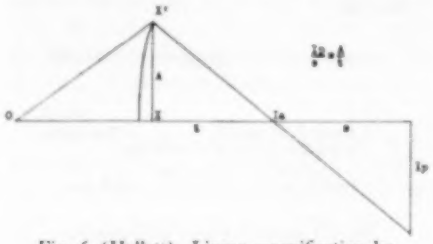


Fig. 6 (Hallett). Linear magnification by sphero-cylinders.

similar right angle triangles, the formula derived is:

$$Ip/A = s/t.$$

If I represents the linear magnification of either one of the two line foci and if t represents the distance from the lens to the other one of the two line foci, then the general formula for linear magnification by sphero-cylinders may be stated as:

$$I/A = s/t.$$

Clarification of these formulas may result from applying them to representative problems. For example, describe the images produced by an illuminated cross 1.0 meter away from a +3 +2D. cyl. ax. 180°, the aperture being 2 cm. (fig. 7).

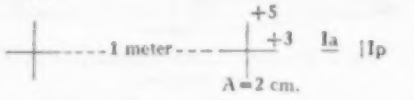
Since the horizontal Ia is refracted through the +5D. vertical planes, Ia must be −1 +5 = +4D. = 25 cm. from the lens; Ip is refracted through the +3D. planes to −1 +3 = +2D. = 50 cm. from the lens; s = 50 − 25 = 25 cm.

$$Ia = As/t = 2 \times 25/50 = 1 \text{ cm.},$$

$$Ip = 2 \times 25/25 = 2 \text{ cm.}$$

$$\frac{Ia}{A} = \frac{s}{t'}, \qquad \frac{Ip}{A} = \frac{s}{t'}, \qquad \frac{I}{A} = \frac{s}{t}$$

Example



Position of—
Ia = −1+5 = +4 D = 25 cm.
Ip = −1+3 = +2 D = 50 cm.

Size of—

$$Ia = \frac{As}{t} = \frac{2 \times 25}{50} = 1 \text{ cm.}$$

$$Ip = \frac{As}{t} = \frac{2 \times 25}{25} = 2 \text{ cm.}$$

Fig. 7 (Hallett). Linear magnification by sphero-cylinders.

By further application of these formulas it becomes a relatively simple matter to study the size of the retinal images in uncorrected astigmatic eyes. For ease of calculation and demonstration on the optical bench let the emmetropic eye be represented by a +6D. lens. This permits us to work on a 10 to 1 ratio, for the dioptric system of the human emmetropic eye averages about 60D. The retina can be represented by a screen 16.7

cm. away from the +6D. lens. This posterior focal length represents the axial length of the emmetropic eye. Let the aperture = 3 mm. to correspond to a 3-mm. pupil.

Consider a 4D. simple hyperopic astigmatism with the rule. Such an eye viewing an illuminated cross 6.0 meters or further away receives the anterior horizontal line focus, Ia, at O +6 = +6D. = 16.7 cm. (fig. 8).

The vertical posterior line focus, Ip, is formed behind the retina at O +2 = +2D. = 50 cm. from the dioptric system:

$$s = 50 - 16.7 = 33.3$$

$$Ia = 0.3 \times 33.3/50 = 0.2 \text{ cm.}$$

By accommodating 4D., Ip falls on the retina and Ia falls at O +10 = +10D. = 10 cm. from the dioptric system:

$$s = 16.7 - 10 = 6.7.$$

$$Ip = 0.3 \times 6.7/10 = 0.2 \text{ cm.}$$

This indicates that the uncorrected astigmatic eye capable of switching from one to the other line focus by appropriate exertion or relaxation of its accommodation receives the same size image in each instance.

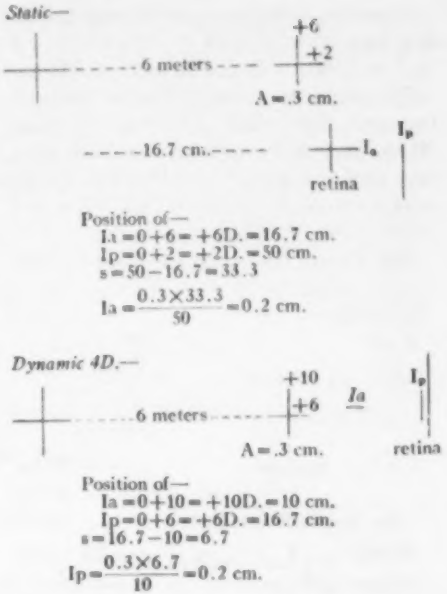
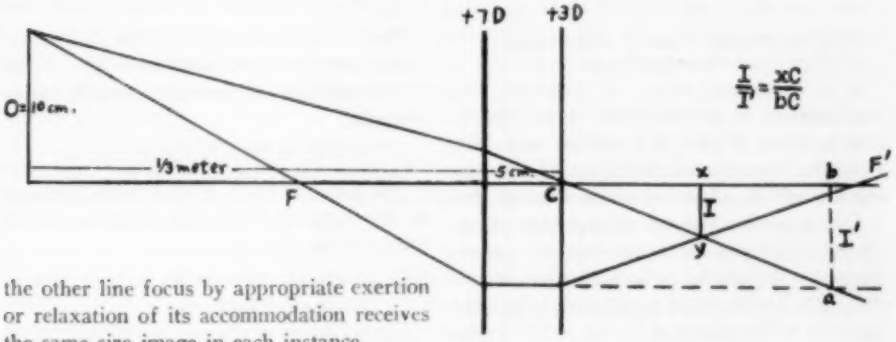


Fig. 8 (Hallett). Uncorrected simple hyperopic astigmatism.



In order to appreciate the effect of cylindrical spectacle lenses on the size of retinal images in corrected astigmatic eyes it is again first necessary to review some basic facts, this time concerning combinations of lenses. For example, a 10 cm. long source of light, O, one-third meter away from a +7D. sph. which is 5.0 cm. in front of a +3D. sph. comes to a focus at 12.5 cm. behind the +3D. sph. (fig. 9).

Position of—
$I' = -3 + 7 = +4\text{D.} = 25 \text{ cm.}$
$I = +5 + 3 = +8\text{D.} = 12.5 \text{ cm.}$
Size of—

$$I' = \frac{Of'}{f} = \frac{10 \times 25}{33.3} = 7.5 \text{ cm.}$$

$$I = \frac{I'(xC)}{bC} = \frac{7.5 \times 12.5}{20} = 4.7 \text{ cm.}$$

Fig. 9 (Hallett). Lens combinations.

According to the vergence formula for the first lens, V = −3, D = +7, V′ = −3 + 7 = +4D. = 25 cm. In other words, the +7D. sph. alone would produce an image 25 cm. away. The +3D. sph., however, being 20 cm. from that image, receives these same rays with a vergence of +5D. Thus, for the second lens V = +5, D = +3, V′ = +5 +3 = +8D. = 12.5 cm.

The size of the image produced by such

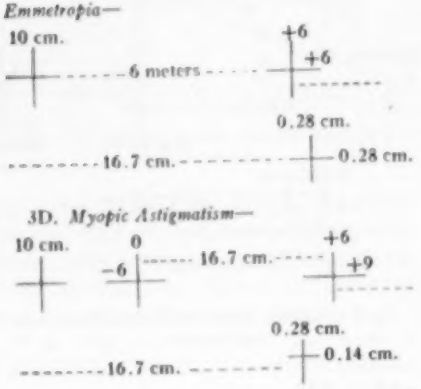


Fig. 10 (Hallett). Size of retinal images in corrected ametropia.

combinations of lenses is very simply determined. From Figure 9 it can be seen that from the extremity of the object, O, there is one ray which, after refraction through the +7D., passes undeviated through the optical center, C, of the +3D. Another ray passes through the anterior principal focus, F, of the +7D. and emerges parallel to the principal axis to be refracted by the +3D. to its posterior principal focus, F′. The image, I, of the lens combination is formed at xy. The image, I′, of the +7D. alone would be formed at ab and its size, in accordance with the formula, I = Of′/f, is 10 × 25/33.3 = 7.5 cm.

From the similar right angle triangles, abC and xyC, the magnification formula for any combination of spherical lenses is derived:

$$I/I' = xC/bC.$$

Applying the formula to the problem at hand:

$$I = 7.5 \times 12.5/20 = 4.7 \text{ cm.}$$

The collapse of Sturm's conoid on the retina of an astigmatic eye effected by the appropriate correcting cylinder converts the original astigmatic system into a stigmatic one which can be resolved by the use of these uncomplicated formulas. For example (fig. 10), a simple myopic astigmatism of 3.0D. against the rule has a far point for the myopic horizontal meridian 33 cm. in front of the eye.

A −6D. cyl. ax. 90° at 16.7 cm. in front of the eye has its posterior principal focus coinciding with that far point and would, therefore, correct the ametropia.

Now, the vertical emmetropic meridian of the eye is unaffected by the zero dioptric strength in the axis of the correcting cylinder, so that a 10cm. object 6.0 meters away will produce the vertical dimension of the retinal image the same size as in the emmetropic eye in accordance with the formula:

$$I = Of'/f = 10 \times 16.7/600 = 0.28 \text{ cm.}$$

The −6D. horizontal meridian of the correcting cylinder produces an image, I′, at the far point also in accordance with the same formula:

$$I' = 10 \times 16.7/583.3 = 0.28 \text{ cm.}$$

The latter image is related to the horizontal dimension of the retinal image in accordance with the formula:

$$I/I' = xC/bC. \quad I = 0.28 \times 16.7/33.3 = 0.14 \text{ cm.}$$

Thus, the size of the image on the retina of a corrected astigmatic eye will differ in the two principal meridians and, just as in spherical ametropia, each dimension will vary in size depending upon the position of the correcting lens in front of the eye. For instance, in the example just cited the closer the correcting lens is placed to the eye, the weaker it would have to be and the larger would be the horizontal dimension of the image.

It is not intended to imply from these theoretic demonstrations that human eyes receive nice sharp retinal images. The well-known inherent aberrations of the eye do not permit that. This in no way impairs the validity and usefulness of the magnification formulas in spherical ametropia, nor should it for the corresponding formulas in astigmatism.

Accordingly, we may conclude that cylinder magnification, unlike spherical magnification, is independent of the size of the object. It is, however, directly dependent upon the aperture of the system.

In simple astigmatism the anterior and posterior line foci, if and when they can be focused by the unaided eye on the retina, are of the same size and are produced in accordance with the cylinder magnification formulas. Corrected astigmatism constitutes a compound spherical system producing a retinal image of unequal dimensions corresponding to the differences in magnification through the unequal meridians of the dioptric system.

Medical Arts Building (2).

CORTICAL POTENTIAL CHANGES IN AMBLYOPIA EX ANOPSIA*

A PRELIMINARY REPORT

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Amblyopia ex anopsia has been known since the days of Hippocrates. Rational treatment was inaugurated by Buffon in 1743, when he suggested the occlusion of the sound eye in order to force the squinting eye into use. Donders, in 1864, insisted upon the use of lenses also. In 1900, Claude Worth turned attention to the cerebral element of fusion, and loosed a beehive of activity in this field.[1]

Since that time, workers in ophthalmology, physiology, and allied fields have gathered information on this subject. Two theories stand out as the product of this effort:

1. That the amblyopic eye ceases to function normally, its physiologic processes are slowed, and its blood supply decreased.[2]

2. Amblyopia ex anopsia develops from a suppression into an active inhibitory reflex. An inhibitory reflex is called into use because of the distracting result of simultaneous stimulation of disparate retinal points in the two eyes. Foveal inhibition must be the most marked.[3]

What evidence is given for these theories of retinal block or cerebral suppression? Abraham,[4] in 1932, showed that hypotonia may result following withdrawal of aqueous from an amblyopic eye by anterior chamber puncture. Hypertonia is the result in a normal eye. In 1937, after an extensive search of the literature, Abraham[5] reported that acute glaucoma is a rare occurrence in an amblyopic eye. (He found only one case in addition to one he reported.) In the case he reported, acute glaucoma followed surgery on the good eye. In the other case, the attack was precipitated by four-percent homatropine in the eye. From these observations, he theorized a decreased blood suppy to the amblyopic eye because of the decreased function.

In 1944, Wald and Burian reported that the retina of the amblyopic eye functions as well as the dominant eye, using the threshold of light as their test. They state that only form sense was suppressed; therefore, the cause of the amblyopia must be in the brain.[6]

Callahan and Redlich, in 1946, did electroencephalographic studies on 10 cases of amblyopia ex anopsia, apparently in adults, and found no difference between the occipital

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rhythm of these cases and normal individuals. They reported only on the occipital rhythm.[6]

Thus evidence and opinion is divided upon the question of whether amblyopia is due to retinal or to central factors.

Method of Investigation

A modern Grass eight channel electro-encephalograph was used throughout. Needle electrodes were arranged in a parallel manner, extending from the frontal to the occipital areas bilaterally. In several cases in which coöperation was obtained with difficulty, only four electrodes were employed. In the great majority of cases, however, coöperation was excellent. Both monopolar and bipolar leads were used.

Patients were placed in a comfortable reclining chair with legs extended, eyes closed. Callahan and Redlich[6] showed that having the eyes open affects the electrical potential of the occipital cortex in such an irregular manner that interpretation of the electroencephalogram is very difficult. By having the eyes closed, the irregular effect of visual stimulation is avoided. In two respects our method differs from that used by Callahan and Redlich:

1. They studied adults. We studied children as well as adults.

2. They did not study the effect of hyperventilation. We studied the effect of hyperventilation.

Cases Studied and Results

We studied 33 cases of amblyopia ex anopsia associated with strabismus; 28 of these cases were in children between the ages of 4 and 14 years; five cases were in adults between the ages of 17 and 30 years. Associated disturbances were also studied. Among the patients studied were eight cases of anisometropia with no history of strabismus, but with decreased visual acuity; three cases of alternating esotropia; two cases of alternating exotropia; four adults, who developed muscle imbalance and suffered from diplopia; and three young patients with pathologic differences between their eyes.

In 28 cases of amblyopia ex anopsia with strabismus in children, 24 had abnormal cortical wave patterns. In four of these cases the electro-encephalographic tracings were normal. In the tracings for the five adults, only one showed abnormal waves; and these occurred after hyperventilation.

TABLE 1

A statistical survey of electro-encephalographic findings in the cases studied

	Amblyopia with Strabismus		Amblyopia with Anisometropia	Alternating Strabismus	Diplopia in Adults
Age (years)	4 to 14	17 to 30			
No. Cases	28	5	8	5	4
Positive E.E.G.	24	1	3	1	0
Percent Positive	86%	20%	38%	20%	0%

In the eight cases of anisometropia with no history of strabismus but with decreased visual acuity in one eye (approximately 20/40 to 20/120), three showed abnormal cortical potentials. In the cases of alternating strabismus, only one patient had an abnormal tracing.

In the adults with diplopia the electroencephalograms were normal. As a general rule, we found that the tracings in adults were normal.

In the tracings of the three children with pathologic changes which would cause different retinal images, the tracings were positive; that is, the brain waves were abnormal.

In no case was there a history of fainting, encephalitis, syncope, convulsions, or other central nervous system disease. All family histories were likewise negative. A history

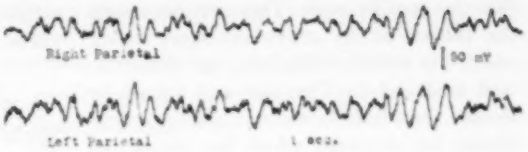

Fig. 1 (Dyer and Bierman). Exotropia with amblyopia ex anopsia. Patient, aged seven years. Vision: O.D.: 20/15; O.S., finger counting. Tracing shows brief bursts of slow waves with increased amplitude.

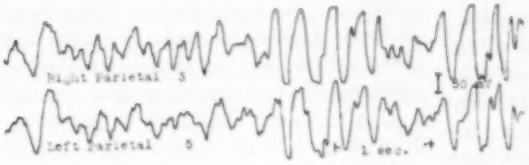

Fig. 2 (Dyer and Bierman). Esotropia with amblyopia ex anopsia. Patient, aged 10 years. Vision: O.D., 20/19; O.S., 20/75. Tracing shows runs of very high amplitude, three to four per-second waves.

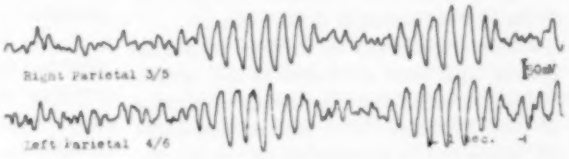

Fig. 3 (Dyer and Bierman). Esotropia with amblyopia ex anopsia. Patient, aged 8 years. Vision: O.D., 20/10; O.S., 20/120 to 20/75. Tracing shows runs of very high amplitude waves with marked slowing and with low amplitude very fast activity interposed.

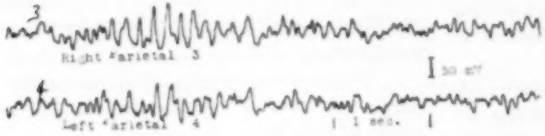

Fig. 4 (Dyer and Bierman). Esotropia with amblyopia ex amopsia. Patient, aged 8 years. Vision: O.D., 20/20; O.S., 20/120. Tracing shows bursts of very high amplitude waves, together with low-amplitude fast activity.

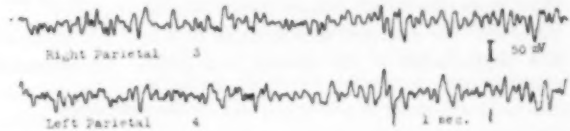

Fig. 5 (Dyer and Bierman). Anisometropia. Patient, aged 10 years. Vision: O.D., 20/120; O.S., 20/20. The tracing is normal.

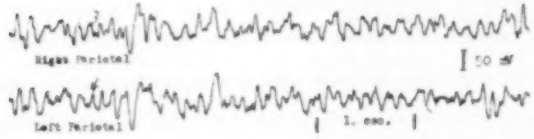

Fig. 6 (Dyer and Bierman). Anisometropia. Patient, aged 10 years. Vision: O.D., 20/100; O.S., 20/20. A mixed dysrhythmia with many high amplitude slow waves.

of enuresis was obtained in one case.

Since, in our cases the electro-encephalographic findings are generalized, the accompanying figures show only the parietal areas. Figures 1, 2, 3, and 4 are examples of abnormal electro-encephalographic tracings obtained in cases of amblyopia ex anopsia. Figures 5 and 6 are cases of amblyopia with anisometropia and no strabismus; the tracing in Figure 5 is normal; that in Figure 6 is abnormal.

Discussion

In the majority of cases of amblyopia ex anopsia in children, we found a widespread active cortical potential disturbance. It was constant and, in our cases, did not require

that the eyes be open. This correlates with the theory of an active inhibitory reflex which has become obligatory, the theory so well advanced by Chavasse and quoted by Scobee.[7] In adults, however, apparently some change has occurred which has altered the condition, for the abnormal waves disappear in the majority of cases. Even when adults develop diplopia, the abnormal waves do not occur. The diplopia, however, does not disappear, and the adults are uncomfortable. There appears to be a definite difference between children and adults, with amblyopia or diplopia, and this difference is expressed in the cortical potential disturbances.

Behavior problems of children with strabismus have been attributed to the psychic trauma to which they are subjected because of their disability. Now the question might be considered as to whether or not the behavior is due to a cortical irritability, for the electro-encephalographic tracings are similar in many ways to those found in convulsive patients.

The three children with a pathologic difference between their two eyes also had abnormal electro-encephalographic tracings. In these cases, the retinal images were obviously different. We interpret this to mean that active suppression of the images in a pathologic eye may contribute to the decrease in visual acuity.

Summary

1. We have found an active cortical potential disturbance in 86 percent of children with amblyopia ex anopsia associated with strabismus. A smaller number (38 percent) of children with amblyopia associated with anisometropia and no strabismus also had abnormal electro-encephalographic tracings.

2. Adults with amblyopia do not have a high percentage or marked E.E.G. abnormalities. In four cases of diplopia, no abnormalities were noted.

3. We believe that our findings lend support to the theory of an active cortical suppression of the form sense in children, but that some change may occur on growing into adulthood.

4. Perhaps the abnormal cortical excitability accounts for some of the behavior problems in the children having suppression amblyopia.

5. Suppression may contribute to a pathologic condition in decreasing the visual acuity of an eye.

6. Much work remains to be done before any conclusions can be accepted as final.

Firmin Desloge Hospital.

References

1. Duke-Elder, W. S.: Practice of Refraction, St. Louis, Mosby, 1943.
2. Abraham, S. V.: Glaucoma in amblyopia. Am. J. Ophth., **19**:1094, 1936.
3. Scobee, R. G.: Oculorotary Muscles. St. Louis, Mosby, 1947.
4. Abraham, S. V.: Anterior chamber punctures in relation to intraocular tension. Arch. Ophth., **7**:888, 1932.
5. Wald and Burian: The dissociation of form vision and light perception in strabismic amblyopia. Am. J. Ophth., **27**:950, 1944.
6. Callahan and Redlich: Electroencephalography and ophthalmology. Am. J. Ophth., **29**:1522, 1946.
7. Scobee, R. G.: Oculorotary Muscles. St. Louis, Mosby, 1947.

AMBLYOPIA FOLLOWING POSTTHYROIDECTOMY HEMORRHAGE*

Relieved with stellate ganglion block and intravenous procaine

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Loss of vision following large distant hemorrhage is comparatively rare considering the great number of individuals who incur great loss of blood. It is most frequently seen following hemorrhages from the stomach, duodenum, uterus, and lungs.

Duke-Elder[1] and Walsh[2] state that the condition is usually seen following bleeding from medical conditions, and is relatively rare from wounds or surgical procedures. It has also been noted that several small, recurrent hemorrhages were more prone to lead to amblyopia than a single, large hemorrhage. Tersen,[3] in 1922, surveyed the literature up to that time and accounted for some 250 cases. Since then, many other cases have been reported, mostly following gastric hemorrhages, nasal hemorrhages, and uterine hemorrhage.

Review of condition

Pathogenesis

Duggan[4] explains the pathogenesis of this condition as being due to a liberation of toxins, probably epinephrine or epinephrine-like substances, which cause a spasm of the central retinal artery. This is followed by a vasodilatation of the capillaries and a liberation of histamine or histaminelike substances, a diffusion of colloids and fluids into the tissues, and retinal edema. If this lasts long enough, there is a loss of blood between the endothelial cells of the capillaries, and hemorrhages and exudates result. Before 1943 and Duggan's studies, therefore, very little of the pathogenesis of this condition was known, although it had long been suspected that some toxic substance had to be present in addition to the hemorrhage.

Pathology

Pathologically, the condition has been fairly well analyzed, though pathologic specimens have not been too frequent. It is generally agreed that there is a degeneration of the ganglion cells with cystoid bodies in the nerve-fiber layers. There is usually a marked retinal edema and occasionally hemorrhages. There may be fatty degeneration of the optic nerve. The arteries are usually markedly attenuated, and the veins are dilated.

Defect in vision

The amblyopia or amaurosis usually comes on between the 3rd and 7th day following the hemorrhage, but sometimes is delayed.

The resulting defect in vision is frequently bilateral, the unilateral cases constituting about 15 percent of the cases reported. The prognosis in these cases has been notably poor. Tidy[6] stated that one third regain no vision. Duke-Elder[1] was of the opinion that 50 percent remain permanently blinded, and only five percent or six percent regain normal vision.

Treatment

The usual treatment called for immediate blood transfusion, but more recently Duggan[4] and Gifford[5] have recommended the use of the vasodilators such as amylnitrite, papaverine, sodium nitrite, small doses of typhoid and nicotinic acid, and paracentesis to reduce the introacular pressure.

The case to be reported presents two unusual features. A severe amaurosis developed

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following a massive hemorrhage after thyroidectomy and restoration of vision was accomplished after several days by the use of stellate ganglion block and intravenous procaine.

Report of case

History. The patient, a man, aged 23 years, was admitted to the U. S. Veterans Hospital on January 4, 1949, with a history of excessive perspiration, nervousness, tremor, and loss of weight of three years' duration. He had been treated privately with 100 mg. of propyl-thiouracil and 30 drops of Lugol's solution daily for four months prior to his admission.

Physical examination revealed a well-developed white man, with warm moist skin. The heart was normal except for a moderate tachycardia of 135 per minute. The thyroid gland was diffusely enlarged.

Ocular examination. The vision was 20/20 in each eye without glasses. He revealed a mild refractive error in each eye. The external examination revealed normal lids and lid margins; the conjunctiva was mildly injected; the pupils were three mm. in size, equal, and reacted well to light and accommodation. The ocular motility was normal, there was no diplopia. The fundi revealed clear media; the discs were normal in size, shape, and color. The vessels were normal in caliber, the ratio of the veins to the arteries was 3:2. There were no hemorrhages and no exudates. The maculas were normal. Von Graefe's lid-lag test was positive, a wide rim of white sclera being exposed as the patient followed the downward excursion of the finger. Stellwag's sign and Dalrymple's sign were present. Convergence was poor. Measurement of the exophthalmos was 27 mm. in each eye (Luedde).

Laboratory studies revealed: Hemoglobin, 13.5 gm.; normal white and differential. The E.K.G. and chest X-ray films were normal. The basal metabolic rate was plus 50 and plus 70.

Treatment. The patient was placed on propyl-thiouracil and on February 25, 1949, the basal metabolic rate was found to be plus 17. On March 2, 1949, the propyl-thiouracil was discontinued and Lugol's solution was given. On March 15, 1949, a subtotal thyroidectomy was performed. On that very same afternoon severe bleeding from the remnants of the thyroid tissues ensued, and the patient went into acute respiratory failure. The wound was re-opened as an emergency procedure and endotracheal intubation was done. The bleeding vessels were found and ligated. The following day (24 hours) the patient complained of photophobia, and on March 16, 1949, he was seen in consultation.

Ocular examination. Bedside examination revealed a severe hyperemia of the conjunctiva, especially on the right, mucoid secretion, but no staining of the corneas. The patient did not complain of visual difficulties. Four days later he complained of sudden loss of vision in each eye, most marked in the right. His vision was recorded as counts fingers at three feet in the right eye, and 20/400 by using eccentric vision. The left eye revealed light perception and faulty projection.

The usual picture of dilated and fixed pupils was noted. The vision was found to be 20/400 in the right eye and light perception in the left eye. The fundi revealed a striking picture of anemia and ischemia. The discs were normal in shape, no edema, and possibly less rosy pink than when seen preoperatively. Both retinas were extremely pale in color. The arteries were markedly constricted and straight, the veins appeared full. There were no hemorrhages and no exudates. Both maculas revealed finely radiating lines suggestive of edema.

The left eye was most striking. The picture here was that seen typically in obstruction to the central retinal artery. The area between the macula and the disc and bordered by the superior and inferior temporal arteries was markedly opaque and presented a "cherry red" spot in the macula.

Blood transfusion was immediately ordered, and the patient was placed on nicotinic acid, 100 mg., four times a day, erythryl tetanitrate, 0.5 gr., four times a day.

On March 24, 1949, three days later, examination of the discs revealed a picture that was not much changed from the original one, with the exception that the left macula showed numerous, fine pigment deposits. There had been no improvement in vision up to this time. It was then decided to use a stellate ganglion block and intravenous procaine.

On March 25, 1949, he was given a bilateral stellate ganglion block. Within 10 minutes the vision in the right eye improved so that he was able to read J2 in bed. In order to maintain the vasodilatation, he was also given 1,000 cc. of 0.1-percent procaine intravenously.

The vision in the left eye remained the same. The visual field revealed a marked temporal constriction, but less than that seen before the injection. The patient refused further treatment with novocain, and was continued on oral vasodilator therapy.

Six days later the fundi revealed normal discs, the right fundus now showed many small pigmentary deposits throughout the periphery. The retinal vessels appeared to be normal in caliber, the ratio of veins to arteries was 3:2. There was no evidence of retinal edema. The left fundus revealed numerous pigment deposits throughout the periphery, and marked deposition in the macular area. The arteries were markedly constricted, the caliber ratio of the veins to arteries was 4:1.

The visual field for the right eye now showed a fairly large scotoma about 35 degrees in diameter, temporal to the fixation area.

One month later the vision remained 20/20 in the right eye and light perception in the left eye. The fundi appeared exactly the same as on the previous examination, and the patient continued the oral vasodilator therapy. The pigmentary migration and proliferation were indicative of permanent retinal damage, and it was believed that the patient had received his maximum therapeutic benefits.

Technique of intravenous therapy

The technique advocated by Graubard[12] and his associates was the method employed. Five cc. of 20-percent solution (one gm.) of procaine hydrochloride is added to 1,000 cc. of isotonic saline solution. This is agitated thoroughly to insure uniformity of solution. The solution is administered by the intravenous route using the drop method and adjusted so that the rate of flow is between 60 to 75 drops per minute. A more rapid administration may result in toxic reactions. The procaine used intravenously is not an anesthetic but an analgesic. Within a few minutes after the start of the infusion, the patient feels a sensation of warmth and relaxation.

Comment

The use of intravenous novocain was stimulated by the excellent results we have noted in another study concerning its use in the treatment of certain painful ocular diseases wherein a high degree of ciliary and vascular spasm was present.[13] Graubard had previously established the effects of inflammation elsewhere in the body, and he believed that a reflex vascular pattern is established at the site of the inflammation. This results in local vasospasm and capillary dysfunction. Graubard found that by using intravenous novocain an immediate local vascular relaxation could be obtained.

The case reported presented an instance of severe retinal vasospasm approaching the degree of total obstruction of the central retinal artery in each eye. As far as is known this type of amaurosis has not been reported following massive hemorrhage following thyroidectomy. The retinal picture, however, was that typically seen in instances of severe bleeding from lung, stomach, and uterus.

The usual vasodilator therapy apparently

was of no beneficial effect in relieving the vasospasm. As a last resort, stellate ganglion block and intravenous novocain were administered. Ten minutes after the ganglion block was done the patient was able to see from the right eye. In order to effect further vasodilation, an intravenous procaine injection was given. The intravenous novocain infusion lasted about four hours.

During this period the patient was able to read J2 with ease from the right eye, but the vision in the left eye was not perceptibly changed. In as much as the left retina had already developed morbid changes it seems probable that a beneficial effect might have been obtained had this therapy been used sooner. The right eye, which up to this point, showed no pigmentary disturbances but merely an angiospastic state, responded at once. The pigmentation that was noted later indicated that a partial destruction of retinal tissue had occurred from the several days of hypoxia that had existed prior to the therapy.

The relative effect of the intravenous procaine cannot be interpreted at this stage but, since the first return of visual acuity was noted at the time of the stellate ganglion block, it is felt that this was probably responsible for the beneficial effect that was obtained.

The use of intravenous novocain in the treatment of ocular conditions is not entirely new. Lundy[7] first used this method for relief of itching in jaundice in 1942. Lorofi[8] used it in the treatment of visual disorders from tryparsamide. Gerbosi[9] and Ezes[10] used it in amaurosis following streptomycin therapy.

In this country the use of intravenous novocain has been confined largely to the treatment of arthritis, infections, and burns. Graubard, Robertozzi, and Peterson[11] used intravenous novocain in over 2,000 cases without serious ill effects. These workers state that when novocain is injected intravenously it becomes hydrolyzed to para-amino-benzoic acid and diethylaminothanol. The stellate ganglion block has been extensively used to paralyze the sympathetic chain to the carotid plexus, thus resulting in vasodilatation of the cerebral arteries.

Stellate ganglion block or cervicothoracic sympathetic block has been used to relieve vasospasm of the upper extremity, head, face, and of the heart. The stellate ganglion is a fusion of the inferior cervical and the first thoracic ganglion. It lies behind the vertebral artery in the space between the transverse process of the seventh cervical vertebra and the neck of the first rib. If the block is successful, a Horner's syndrome results.

This case presented the usual signs of miosis, enophthalmos, narrowed palpebral fissure, and hypohidrosis of the face and arms. There was also an injection of the conjunctiva.

Both the stellate ganglion block and the intravenous procaine injection were performed and administered by Dr. Rocco Tella of the anesthesiology staff. Each stellate ganglion was reached by the lateral route, and five cc. of one-percent procaine in oil was used.

Conclusions

An unusual condition of amaurosis following massive hemorrhage from a thyroidectomy was relieved in one eye immediately after stellate ganglion block and intravenous procaine injection. In view of the angiospastic state of the retinal vessels it is evident that these procedures afforded an immediate and marked vasodilating effect. It is likely that the individual or combined procedures may be useful in several other conditions characterized by vasoconstriction or obstruction of the retinal arteries. The selective action of intravenous novocain to the site of vasospasm caused by painful sensory sitmuli offers an opportunity to study this mechanism in a variety of ocular diseases.

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References

1. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, Mosby Co., 1942, v. 3.
2. Walsh, F. B.: Clinical Neuro-Ophthalmology. Mosby, Baltimore, Williams & Wilkins, 1947.
3. Tersen, A.: Ann. d'ocul., 159:23, 1922.
4. Duggan, W. F.: Clinical vascular physiology of the eye. Am. J. Ophth., 26:354-68, 1943.
5. Gifford, S. R.: Tr. Am. Acad. Ophth., 48:19-30, 1943.
6. Tidy: Brit. M. J., 6:274, 1941.
7. Lundy: Clinical Anesthesia. Philadelphia, Saunders, 1942.
8. Larofi, H.: Presse méd., 55:435, 1946.
9. Gerbosi and Burgio: Gior. di med., 4:99-103, 1947.
10. Ezes, H.: Bruxelles-méd., 28:1977-2032 (Sept.) 1948.
11. Graubard, Robertozzi, and Peterson: New York State J. Med., 47:2187-91,
12. ———: Anesth. & Analg., 27:222, 1948.
13. Grossmann, E. E., Hitz, J. B., and Roncke, G. J.: To be published.

SQUINT AMBLYOPIA: ITS NATURE, DIAGNOSIS, AND EFFECTIVE TREATMENT*

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Numerous efforts have been made to arrive at a clearer notion concerning the true nature of amblyopia ex anopsia and the reason for its development.

Wald and Burian,[1] from intensive study of five individuals having strabismic amblyopia demonstrated that the light threshold of the amblyopic eye was normal, both at fovea and periphery, and in light and dark adaptation. Further, they found that these patients have capacity to fixate lighted objects with the affected eye. On the strength of these findings, together with the fact that some lower animals retain their capacity to see light, their power of brightness discrimination, and their sense of space localization after removal of the occipital cortex, Wald and Burian concluded that there must be present in amblyopia ex anopsia a defect in pattern vision. They consider pattern vision to be a cortical function and suggest that the amblyopia results in cortical inhibition of the function of pattern vision, involving principally its macular projection on the cortex.

This thought suggests that we may have been seeking a too complicated explanation of altered physiology involved in producing the protective devices against diplopia of squint. Suppression, anomalous sensorial relationship—also known as false projection or anomalous retinal correspondence—and amblyopia ex anopsia comprise this group, of which squint amblyopia is the only one formerly considered to involve actual organic changes.

Nature of amblyopia ex anopsia

Suppression is a psychic faculty of control, unconsciously made daily use of by all of us. It serves many purposes: ignoring the image of the unused eye at a monocular microscope; closing our hearing to sounds about us as mental powers are concentrated upon some specific problem; blotting out visual impressions when listening intently; getting clear visual perception when using a head mirror for nasal or aural work; or in use of the endoscopic tube in any of its applications. Suppression is a fleeting thing, always at hand, readily applicable to either eye or to both with instantaneous facility. To overcome its specific application is a matter only of drawing the individual's attention to

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the situation and of inducing his recognition of its undesirability. Being basic, but unstable, it may be the primary condition out of which each of the other escape devices evolves.

Binocular function is not present at birth, but grows toward perfection as the individual matures in capacity for complex visual action. It seems likely that stereopsis and depth perception are not generally established before the age of three years. During this early period of unsettled visual habits even a mild interference may leave its mark upon the final picture, and definite diplopia for only a few weeks could seriously alter the end result. Occurrence of diplopia at the onset of squint seems a logical supposition. That it often arouses an intense subjective disturbance, too, is attested by the sudden irritability, crying, rubbing of the eyes, and stumbling when trying to move about exhibited by young children who abruptly develop frank strabismus. We do not often realize this stage of psychic upset in our young squint patients because parents are lacking medical powers of observation, and because our history taking is usually too superficial.

The extent of response from nervous tissues is bounded by an innate threshold of stimulation peculiar to each particular structure.[2] The ocular apparatus is no exception,[3] and it appears logical that this threshold should be purposely high during the earliest year or two of life, with a gradual lowering of its level as coördination of ocular neuromuscular mechanism comes about, and as the developmental process in retinal structures is completed.[3, 4]

Also, during that period, alteration or delay of threshold lowering could presumably occur in any part of the ocular apparatus that was retarded in assuming its proper role in binocular perception. Thus an eye that constantly deviated, because of its lack of dominance in a squint, might readily retain the infantile threshold of stimulation. It would be natural, too, for that level of tissue unresponsiveness to be accentuated as psychic development progressed, and for such an eye to become intensely amblyopic without any structural abnormality of its seeing elements. Being functional, this condition would be amenable to education and could be overcome to a degree depending upon the individual's psychic adaptability and upon effectiveness of the method adopted for reëducation. Perhaps the last statement is also subject to some further limiting factors.

Development of amblyopia

Ludvigh,[5] and Wald and Burian[1] suggest that those persons developing amblyopia ex anopsia first lose visual acuity then light differential sensitivity. When the latter stage is reached, Ludvigh believes that occlusion of the sound eye is unlikely to improve visual acuity of the amblyopic one. Thus the depth or stage of development attained by strabismic amblyopia may have a bearing upon the end result of treatment. It is of interest, though, that this does not seem to be influenced by how long the amblyopic state has existed after it has become fully established.

In other words, the patient, aged seven years, with visual acuity of 10/800 in his crippled eye is likely to show the same visual level at the age of 20 or 30 years. Apparently this condition follows an individual pattern, just as degree of response to drugs, excitement, shock, and fatigue do. The amount of visual depression in amblyopia ex anopsia seems not to increase with added years—at least short of the period where senescent failings, such as presbyopia, begin to appear.

As to why one or another of the escape devices is adopted by a given patient, it is not possible to say with any certainty. If we accepted the physiologic explanation given, it would seem to depend upon: (1) The age at which the squint appeared and (2) the degree of innate determination of the individual toward retaining binocular function. Thus onset of squint at birth, or within

2 or 3 months thereafter, in one whose natural inclination for stereopsis was not a strong inheritance, could easily lead to suppression of the image of one eye all the time and produce a monocular squinter.

At a little later period, but still within the time when development processes are going on, a similar situation might be expected to result in anomalous retinal correspondence, not because of any anatomic peculiarity but from the fact of greater advancement toward the ultimate goal in development of retinal structures and psychic processes. Suppression, on the other hand, may be made to suffice after a degree of physical and psychic self-determination has been attained.

Accurate diagnosis

Accurate diagnosis of amblopia ex anopsia is of utmost importance, and serious mistakes do occur. A boy, aged 10 years, with unilateral juvenile macular degeneration was judged by an able ophthalmologist to have squint amblyopia because of convergence excess considered to be the remnant of a tropia. Treatment was instituted by the usual occlusion of his sound right eye and he wore the patch 12 months before his parents became discouraged and sought help elsewhere. A more common error is to discourage an already depressed young adult victim of squint amblyopia with the verdict that surgery for cosmetic purposes is all that can be done.

Taken with the actual presence of strabismus, a history of strabismus having formerly existed, or indications in examination data of such a history, the following statements of Luther C. Peter[6] upon this subject are still of determining importance:

"Amblyopia is of frequent occurrence in monocular esotropia. In fact it is largely confined to this form of concomitant squint. It is not present in the alternating type and but rarely in exotropia.

". . . The following facts are evident: (1) The amblyopia is limited to the macula and consists of a scotoma 2 to 3 degrees in diameter; (2) it is a relative area, indistinct for white and never absolute, even when central vision is very low (light sense is preserved); (3) it has been shown in recent studies that treatment improves even the most profound cases, although the degree of improvement depends upon the duration of the scotoma, the age of the patient, and the degree of central visual acuity; (4) there is a relative increase in the size of the blind spot of Mariotte; (5) peripheral fields in the amblyopic eye are smaller than the fields of the fixing eye."

The nature of a central scotoma demonstrated in suspected amblyopia ex anopsia is of utmost diagnostic importance. Walsh[3] discusses division of these cases into two types. One with visual acuity of 20/200 or better where it is always possible to chart a small central scotoma; and another where vision reaches extremely low levels, with pronounced eccentricity of fixation, and roughly circular central scotoma which is larger and denser than that found in the first group.

More systematic study of patients with squint amblyopia is needed to clarify this point, as there seem to be many cases of lesser degree that have no central scotoma even for blue, by ordinary office methods. Other cases clearly show central scotoma for blue only, and comparatively few exhibit relative scotoma for white. Beyond question, we should seriously doubt any diagnosis of amblyopia ex anopsia when there is an absolute central scotoma.

Treatment of squint amblyopia

Generally speaking, two features characterize the established treatment of squint amblyopia: "Continuous occlusion of the sound eye is the only thing of any importance," and "unless begun during childhood or early teens it is of no value."

Valid objections may be raised to both conclusions: (1) To occlude the better eye of a patient with very poor visual acuity in the other largely robs him of his ability to protect himself against accidental injury,

both in the home and outside it; (2) such treatment is not often available to more adult individuals for economic reasons, since one can scarcely carry on any form of occupational activity to advantage with a visual acuity of even 20/200; (3) in infancy and early childhood, vision of the occluded eye must be watched to prevent it from becoming the amblyopic one; (4) continuous occlusion is difficult to maintain because, to be effective in a child, it must involve some form of adhesive dressing that will soon prove both irksome to the child and irritating to his skin; (5) most individuals will not tolerate its restriction of their activities; (6) unless carried to a reasonable degree of completeness the benefit gained may be lost;[1] and (7) continuous occlusion of the sound eye is a passive process, succeeding only to the extent that active effort is put forth to see with the amblyopic eye.

Beyond question, the underlying mechanism of this condition is a psychic one. Application of urgent desire and determination to overcome it is therefore logical. For 10 years I have followed a plan of inducing active effort with the amblyopic eye. Occlusion of the unaffected eye is carried out only during exercise periods, which occupy 1 to 2 hours daily or twice daily. Treatment is not, as a rule, begun until the patient can be made to understand its purpose at which time there is little difficulty in effecting occlusion or in getting full coöperation.

In our early trials, newspapers were used, the individual beginning with large headlines and trying to read those of smaller and smaller type, then the advertisements, and finally ordinary print. Even this simple means gave some surprising results as to near vision, but we found that distant seeing was not keeping pace. Semiweekly visits to the cinema have been adopted, the child being permitted to see the early part of each of his first several shows with both eyes, then the remainder with his sound eye covered. Gradually he comes to view the entire performance with his amblyopic eye. Natural interest in the story stimulates desire to see better, and definite progress in distant seeing is soon achieved.

Innumerable facilities are at hand from which to design suitable exercises. Frequently, after perceiving the method and purpose involved, parents will offer helpful suggestions as to measures available to their particular circumstances.

With young children, the comics or other colored papers may be cut into small pieces of varying shapes and colors which the child is taught to sort into lots as to shape or color using a thumb forceps. Stringing of coarse beads, later of finer ones, and finally of sewing them onto cloth according to simple patterns—always using the amblyopic eye—may furnish many hours of fascinating and spontaneous training. Embroidery, using coarse or fine colored yarns on burlap, is often useful. Cutting out with blunt-pointed scissors, after first tracing the outlines of given subjects, may be employed.

Naturally, one must grade the exercises in accordance with the intelligence, age, and likes of the child. Erector type of toy construction, intriguing patterns of embroidery, practice in writing and printing, drawing, painting of subjects requiring exact application, drawing and burning of designs upon wood or leather, wood carving and clay modeling, all qualify in requiring use of eye and hand together, and in furnishing a creative aspect to stimulate interest. Lazich[7] has offered some interesting suggestions for this particular purpose.

A coöperative parent who will promote and direct the program is essential to the plan. Patients should have reasonably frequent checking by the physician to evaluate progress in visual improvement, answer questions, change activities as need arises, and generally to make clear his interest in the outcome. Periods between these visits may be varied from several weeks to three months, depending upon the patient's enthusiasm of attack, need of the individual for outside urging, and such other factors as

characterize the particular case.

Some question has been raised as to the permanency of results from treatment of squint amblyopia.[3] It appears that there is definite readiness in most cases to accept and to make the most of whatever measure of binocular function is available, if the visual axes are normally directed. This seems true even when considerable disparity in the visual powers of the two eyes still exists.

The question of how long such treatment should be carried out can best be answered by stating that it should be persisted in so long as there is measurable improvement in vision of the affected eye. The degree of recovery to be expected depends upon such factors as: depth or grade of visual depression present, degree of enthusiasm and persistence of an individual's efforts, and whether he is satisfied with less than the ultimate value that can be attained. Some will achieve acuity comparable with that of the fellow eye in the space of several months, and others will improve slowly over several years.

If one is unalterably converted to continuous occulsion, as some orthoptists appear to be, combination of active measures with it will certainly be of advantage in bringing more rapid results.

Whatever validity the much-subscribed-to notion that the age of the patient finally determines how much may be accomplished can no longer be supported as many cases show. Two of my patients are especially interesting in this connection.

A 27-year-old candidate for military enlistment came for examination of his eyes early in 1943. He had been rejected because visual acuity in his left eye was only 3/800. There was a history of monocular strabismus during infancy and early childhood. The right eye was normal, and the left showed no visible organic change but conformed to diagnostic requirements of squint amblyopia. This patient eagerly accepted the notion that he might improve his crippled vision and went to work. Eight months later, he wrote from a distant state to say that his left eye had improved to the extent that he had just been accepted for military service.

A nurse, aged 39 years, had monocular strabismus with amblyopia of her left eye permitting vision of 20/553, corrected or not. Fixation of the amblyopic eye was unsteady. Under an intensive program of active effort to see with it, she brought manifest vision of her left eye up to 20/114 in just 40 days.

Such cases, of which many may be cited, illustrate well the fact that adulthood does not preclude the overcoming of amblyopia ex anopsia. They also testify to the greater effectiveness of active treatment as compared with the more passive program usually depended upon.

Summary

Some facts and some hypothetical thoughts are presented as to the origin and nature of amblyopia ex anopsia.

Importance of more careful diagnosis in these cases is stressed, and a tentative diagnostic formula given.

Active treatment, as opposed to passive occlusion of the sound eye, is described, and its advantages pointed out.

Age as a factor in improving the condition is disputed.

33 East Second Street South.

References

1. Wald, G., and Burian, H. M.: Am. J. Ophth., **27**:950-963, 1944.
2. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice. Baltimore, Williams & Wilkins, 1945, Ed. 4, pp. 781 and 960-961.
3. Walsh, F. B.: Clinical Neuro-Ophthalmology. Baltimore, Williams & Wilkins, 1947, pp. 268-269.
4. Lancaster, W. B.: Fifty years' experience in ocular motility. Am. J. Ophth., **24**:741-748 (July) 1941.
5. Ludvigh, E.: Am. J. Ophth., **25**:213, 1942.
6. Peter, L. C.: Extra-Ocular Muscles. Philadelphia, Lea, 1936, pp. 176-179.
7. Lazich, M. B.: Amblyopia ex anopsia. Arch. Ophth., **39**:188-192 (Feb.) 1948.

IRON PIGMENTATION OF THE PALPEBRAL CONJUNCTIVA*

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Siderosis of the conjunctiva is an unusual condition. Little has been written about it. Koeppe,[1] in 1918, briefly reported several young soldiers showing the local tissue response to metallic foreign bodies of iron in the conjunctiva. With a slitlamp the "metallic-like dark little particles were seen in the conjunctiva and episclera; around these could be seen a profuse deposition of dark yellow to dark rust-brown particles."

The clinical appearance of the case to be reported was nothing like that described by Koeppe. The reason for the difference probably lies in the type of iron to which the patient had been exposed. In this case it was an iron oxide occurring in lateric road dust.

Reese,[2] in 1946, reported the effects of an exogenous pigment, mascara, on the palpebral conjunctiva. These patients were all women who had used this cosmetic on the lashes for a long time. The case to be reported clinically resembles the condition described by Reese.

CASE REPORT

Eye examination. E. H., a 20-year-old army veteran, was treated for a foreign body embedded in the right cornea. For years he has been troubled with moderate excess lacrimation. Vision was 20/20—1 in each eye. A routine examination revealed moderate engorgement of the bulbar conjunctival vessels. The palpebral conjunctiva was quite congested especially above. No excess tearing was present.

There was a low-grade follicular hypertrophy over the upper border of the upper tarsal plates of the lids. There was a peculiar silver grayish pigment discoloration which extended as a band, approximately 2.5 mm. wide, entirely across the upper edge of the tarsal plates. It spread out and was more marked at the nasal and temporal sides. With a loupe it had dirty fine granular appearance with, here and there, clumps of darker collections of pigment. Blanching with a solution of epinephrine (1:1,000) brought out these pigment collections much more strikingly.

Biomicroscopy revealed a definite follicular hypertrophy with deep and superficial pigment granules at the upper tarsal border.

The lower tarsal plates appeared normal as did the bulbar conjunctiva. Deep in the lower fornix, there was definite lymphoid hypertrophy but no visible pigmentation. The rest of the examination was essentially normal.

History. A week later at the staff conference, the patient's history was obtained. Durthe Philippine campaign, he was exposed to heavy dust on an average of at least an hour a day for five months. This occurred while riding in open trucks and was never more than five hours at a time. He found the dust caked heavily around his lid margins on returning to quarters. Later in Korea he drove a truck about 10 times through very heavy dust for from 3 to 4 hours at a time.

Biopsy. A biopsy was taken from the palpebral conjunctiva of the left upper lid over the upper border of the tarsal plate.

The specimen was fixed in formalin. Routine sections stained with hematoxylin and eosin showed numerous follicles in the conjunctiva. They were composed mainly of lymphocytes and some plasma cells. The follicles were quite vascular. Deposits of brown amorphous pigment granules were found. A few small deposits were present just under the surface epithelium. Cross sections of some follicles showed deposits in their vascular cores. Larger deposits were present at the base of the follicles but the largest de-

* From the Eye Pathology Laboratory of the Massachusetts Eye and Ear Infirmary. This study was aided by the Kresge Eye Pathology Fund. Read before the New England Ophthalmological Society, April, 1949.

Fig. 1 (Chisholm). Photograph of eye blanched with solution of epinephrine (1:1,000) intensifies the large collections of pigment along the upper border of the tarsal plate. The greater amount of pigmentation at the nasal end of the tarsal plate is clearly seen. Attention is also drawn to the dilated conjunctival vessels.

posits were found in the subfollicular stroma just under the follicles. At the bottom of the crypts the pigment was infrequent and in small amounts.

Diagnosis. Follicular hypertrophy of conjunctiva associated with exogenous pigmentation.

Later, sections were bleached but this produced no changes in the granular deposits. Other sections stained with potassium ferrocyanide after Perls's technique gave the characteristic blue color of iron in the deposits.

Dr. Warren J. Mead, professor of geology, Massachusetts Institute of Technology, confirmed my belief that the volcanic soil of the Philippines contained iron. He stated that it was in the form of an oxide. He generously sent in a sample of similar lateric soil from Haiti. The presence of iron was confirmed chemically in the sample of soil.

Experimental. Each week, beginning March 13th, 10 mg. of jeweller's rouge, an iron oxide (Fe_2O_3), were put in the right conjunctival sac of a rabbit twice daily for five consecutive days and once on Saturday. Twenty mg. of Haitian lateric soil were put in the left conjunctival sac in like manner. Both preparations were tolerated extremely well. No conjunctivitis, ulcers, and so forth developed. It was noted that the nictitating membrane cleaned the cornea much as a windshield wiper cleaned a windshield and that the majority of material was soon rolled up in balls.

On June 2nd, 11½ weeks later, a biopsy was taken from the conjunctiva of the upper and lower lids of each eye. Microscopic ex-

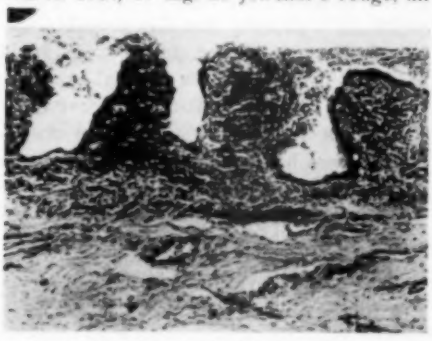

Fig. 2 (Chisholm). Photomicrograph (hematoxylin and eosin) showing the follicular formation of the palpebral conjunctiva.

Fig. 3 (Chisholm). Photomicrograph (low power, Perls's reaction) showing iron deposits especially in the subfollicular stroma. Note the almost complete absence of deposits at the base of the crypt. F = follicle. C = crypt.

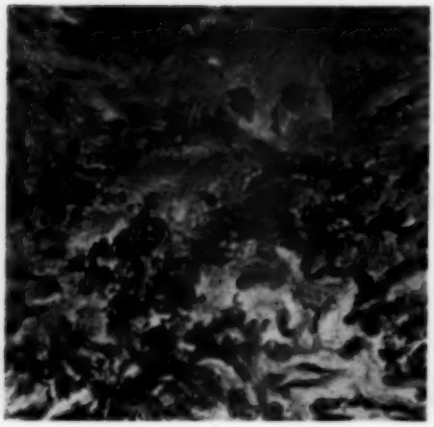

Fig. 4 (Chisholm). Higher power photomicrograph showing the amorphous nature of some of the deposits.

amination of the specimens failed to show either pigment granules or iron reaction. To allow complete healing of the conjunctiva the experiment was not resumed until June 7th.

On July 29th, approximately 19 weeks after the experiment was started, in spite of normal appearing conjunctiva as seen with a loupe, the biopsy was repeated from the conjunctiva of the upper and lower lids of both eyes. In hematoxylin and eosin sections, a few amorphous brown granules were found in the subepithelial connective tissue of the upper lid of the right eye. Sections stained for iron showed neither granules nor iron. Unfortunately, the further sections missed the small areas of pigmentation. The sections from the lower lid were normal.

In sections from the left upper lid somewhat smaller though more diffuse deposits of amorphous brown granules were present deep in the subepithelial connective tissue. Iron staining confirmed the presence of iron in the deposits.

While the experiment did not produce in the rabbit the clinical picture seen in the veteran, yet it did demonstrate that iron could have been introduced in the conjunctiva in that manner. It was felt that the particles of dust constantly flying into the veteran's eye daily over a long period of time were probably more irritating. Another factor is the greater ability and tendency of

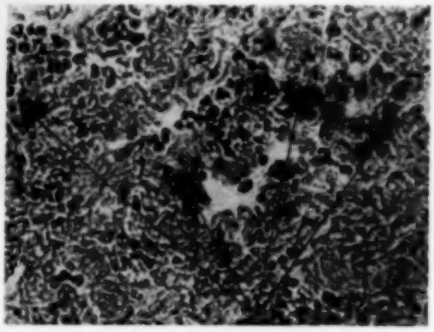

Fig. 5 (Chisholm). Experimental iron deposits (Perls's reaction) in subconjunctival tissue of rabbit.

man to rub his eye in the presence of a foreign body. On the other hand, the rabbit is constantly exposed to dust throughout life. One would expect that his conjunctiva would have developed more resistance to dust.

Summary

Attention is called to a new clinical entity in a veteran, resulting from prolonged exposure to lateric dust in the Philippine campaign. It is thought that this probably was an advanced case. The milder cases could easily be overlooked in a hurried examination. The wide distribution of veterans throughout the country would lead one to expect cases being recognized from time to time in unrelated areas.

An experimental confirmation of the mechanism of the pigment deposition is given.

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References

1. Koeppe: Arch. f. Ophth., 97:27, 1918.
2. Reese: Tr. Am. Ophth. Soc., 44:113, 1946; Am. J. Ophth., 30:1352, 1947.

HEMANGIOMA

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Hemangioma is the most common primary intraorbital growth. A review of the literature of these fascinating pathologic conditions strengthened my opinion that they are all congenital; that predisposition to this type of growth exists at or before birth, and the later manifestations of its presence are merely an overgrowth of the original deformity, producing secondary symptoms by which its existence is made known. It is my belief that many persons have orbital hemangiomas all their lives but, since the tumors remain dormant, their presence is unknown.

It would seem probable that some unusual muscle imbalances might primarily be induced by such a tumor. One of the cases I am reporting had no symptoms whatsoever until the growth's existence became apparent.

These tumors can only be diagnosed by keen clinical observation and with expert laboratory assistance. They are usually unilateral and are capable of producing numerous and varied symptoms due to their positions and extensions in the orbit, and are, indeed, fascinating puzzles. Their exact positions and extension must be known for surgical approach and removal. The different orbital tumors and the pseudotumors caused by systemic diseases or pathologic conditions in the surrounding structures make this an absorbing subject.

CLASSIFICATION OF HEMANGIOMAS

Reese has classified hemangioma into: (1) Capillary, (2) cavernous, (3) angioblastic or hypertrophic, (4) racemose or cirsoid.

The angioblastic type is a solid mass of endothelial cells with no patent vessels or minimum of very small channels. The rapid proliferation of embryonic endothelium eliminates the lumen. The racemose type is composed of a pulsating mass of dilated thickened tortuous blood vessels and proliferating capillaries.

These tumors usually occur in adults with a relatively sudden onset and probably represent an ordinary hemangioma that has established a communication with a surrounding normal artery or arteriole. The communication enlarges and because of constant arteriole pulsation may erode and invade surrounding structures leading often to fatal hemorrhages.

Reese also points out that hemangiomas excepting the racemose type do not show progressive unlimited growth but tend to reach a size and become stationary with full-bodied development. This point should be borne in mind when considering radical, and possibly disfiguring, surgery in the young.

Occasionally there is a spontaneous regression due to the thrombotic occlusion of this tenuous blood supply, consisting of one efferent and one afferent vessel.

G. Renard and G. Offret described three anatomic types of cavernous hemangioma: Cystic angioma, angiolipoma, and hemolymph angioma. They state that simple angioma is not common and is capable of great extension, often being associated with nevus flammeus.

Simple hemangioma having no capsule tends to infiltrate widely in the orbit, menacing the integrity of all the orbital structures; the removal is difficult and is often followed by severe hemorrhage, sensory and motor disturbances.

SYMPTOMS OF HEMANGIOMA

Symptoms of hemangioma are unique, variable, and puzzling. In the early stages of the growth we should expect motor and sensory disturbances, which later become more constant symptoms, and displacement of the eyeball and orbital contents.

Since all tumors occupy space, proptosis is the most constant common sign, but it does not manifest itself in every case. In the earliest stages, the proptosis is usually straightforward but, after a brief period, a lateral or down displacement usually occurs giving some indication of the position of the growth.

Hemangiomas very often become thrombotic, with secondary degeneration. Often, however, orbital hemorrhage occurs, giving cause for surgical exploration of the orbit.

In considering orbital tumors in general we must extend our views a little never forgetting that the eyeball and orbit are not isolated organs and that the body as a whole is our exploring ground.

Vision is usually not affected unless the tumor is very large or situated in the muscle cone, causing pressure on the nerve. This is manifested by the defects in the visual field that usually indicate posterior orbital growths.

Many posterior orbital tumors have an intracranial ramification and, since the preservation of vision with normally functioning eyeball and eyelids is the primary objective in the surgical removal of all orbital growths, the surgical approach is of extreme importance and merits much study. Due consideration must be given to trauma and disfigurement.

Marked ocular limitation seldom occurs but any unusual muscle imbalance that is noticed over a period of years may, in my opinion, be one of the first symptoms of this tumor. However, failure of the growth appreciably to affect the motility of the eyeball is a common characteristic.

Regression of the exophthalmos following irradiation is a symptom of diagnostic value, for this type of tumor is radiosensitive. The rate of growth is also of diagnostic importance—the more malignant the growth the more quickly it enlarges.

Vascular tumors, which more readily travel in the line of least resistance, very often crisscross; that is, their origin may be on the nasal side of the orbit but their external manifestations may be on the lateral side. This type of tumor is usually situated in the posterior or apex of the orbit.

X-ray studies in these conditions are usually negative but, when positive, generally indicate a serious condition. Tumors with arterial pulsation are more prone to cause bone erosion and invade surrounding structures. The differences in density of bone shadow and shadow outline, manifested in expertly taken X-ray films, will materially assist in differential diagnosis.

The X-ray findings often show increased density of the sphenoidal ridge, but this picture of hyperostosis does not necessarily mean extraorbital extension, although there is that probability. Nature's effort to develop tough membranes to prevent the spread of the tumor often confuses the X-ray findings. These shadows frequently suggest a tentative radiologic diagnosis of meningioma, when the real cause could be a cavernous hemangioma.

Vocal resonance could be an aid in the detection of solid tumors. It was pointed out in an article entitled, "Some of the most important ocular and orbital wounds in war," that vocal resonance was increased in the presence of a large metallic foreign body. If a stethoscope is placed over the eye in an orbit that shows a pathologic condition and the vocal resonance is increased, as compared to the normal orbit of the opposite side, it is certainly justifiable to assume the presence of a solid or bony tumor.

The stethoscope is also a valuable aid in ruling out the existence of a solid tumor by permitting detection of bruit. The presence of an arteriovenous aneurysm is definitely established when a loud bruit is encountered. On the other hand, a soft low-toned bruit may suggest a pulsating vascular tumor. One would think that all vascular tumors would pulsate, but this is certainly not the case; the pulsation depends on the growth's histologic makeup.

The presence of pseudotumors, such as tuberculoma of the orbit, and other massive

organized exudations or growths must be eliminated if an exact diagnosis is to be made. A careful history, keen clinical observation, and expert laboratory assistance to make a complete physical examination are essential. Many cases of bilateral exophthalmos are due to a systemic pathologic process but it must not be forgotten that high degrees of unilateral myopia and early hyperthyroidism are not dependent on orbital tumors. Unilateral exophthalmos can also be produced by blood dyscrasia, Mikulicz's disease, and inflammatory diseases of the orbit and accessory sinuses.

Berens states, "intermittent or periodic exophthalmos is attributed to a variety of causes, the most common of which are varicosities of the orbital veins, vascular tumor, hemorrhage, cavernous hemangioma, and recurrent inflammation. The exophthalmos tends to increase or become stationary or to disappear, depending on the disposition of the ideological factor." We have seen in one case of hemangioma of the orbit a symptom which has not been described, a pulsating diplopia.

The variation of the exophthalmos due to variable stasis can be produced by increasing blood congestion in the jugular area by such means as compression, bending, or twisting the head. I have seen one case in which the hemangioma could not be seen under the upper lid but, when the head was bent, there was a marked exophthalmos which persisted while the head was held in this position. The hemangioma could then be seen under the upper lid. Both the exophthalmos and the hemangioma immediately disappeared in this patient upon assuming the erect position. The hemangiomatous nature of the lesion is revealed in the cases I am reporting both subconjunctivally and subcutaneously.

Treatment of hemangioma

The prognosis of most hemangiomas, when they are correctly and early diagnosed, is good. Since they are usually encapsulated and have limited growth, these tumors are very amenable to treatment. When situated in the anterior third of the orbit, they respond satisfactorily to alcohol, sodium-morrhuate injections, and radium.

Generally speaking, hemangiomas in the anterior third of the orbit can be satisfactorily treated with injections or incision; in the middle third, the Krönlein operation is the best approach for incision and treatment; for those existing in the posterior third, well behind the globe, the transcranial approach offers the best method. These tumors often simulate meningioma. Such a finding makes the transcranial exposure essential.

Stallard makes a plea for lateral orbitotomy (Krönlein's operation) for a neoplasm whose physical signs prove conclusively that the entire growth is well within the orbital cavity. He claims that this procedure gives more direct and adequate exposure, and cites a case of a neurofibroma, situated within the muscle cone, which was missed by the transfrontal approach.

It is of interest to study the literature prior to 1925. One is impressed by the gradual increase in knowledge and skill that has taken place. The principal modes of attack in those years were ligation, repeated electrolysis, ignipuncture with a red-hot Paquelin cautery, and injections with alcohol.

Many authors warned against coagulating injections. They state that, in a deep-seated orbital hemangioma, excision is the most desirable treatment, but this is often impossible without an amount of destruction which might be considered scarcely justifiable in dealing with a tumor, the natural tendency of which is innocent. Such means as will cause coagulation of the blood and obliteration of the tumor are to be considered, but because of the danger of septic thrombosis coagulating injections should never be employed without ligation.

Ligation alone of the artery supplying the tumor or of the main trunks going to the part of the body containing the tumor has not proven satisfactory because the collateral

circulation soon causes a return of the growth.

A case has been reported in which the tumor was seen as the swelling of an enlarged blue vein that involved the outer half of the eyelid, including the external canthus, with obliteration of the conjunctival sac. Electrolysis was tried, using the positive and negative current, 5 or 6 times with no result. After three injections of alcohol, however—the first containing three mm., the second, five mm., and the third, six mm., one week apart—there was no evidence of the tumor after the last injection.

Case report

In looking over the history of these early cases, in spite of the incomplete removal of the hemangiomas because of faulty surgical approach, it would seem that a large number of apparent cures were affected, which testify to the benign character of these tumors.

The case to be reported is a spontaneous rupture of a hemangioma of the orbit.

History

The patient, a girl, aged 17 years, presented herself for treatment at the New York Eye and Ear Infirmary on December 27, 1911, with an exophthalmos of the right eye (fig. 1), stating that on December 15th she had suddenly had intense pain in the right eye, accompanied by vomiting, drowsiness, and a bulging of this eye. Two weeks later the following examination was recorded.

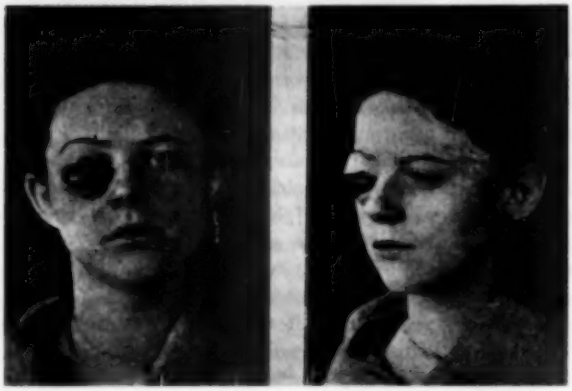


Fig. 1 (Doherty). Appearance of the patient on December 27, 1911, when seen at the New York Eye and Ear Infirmary. (Reported by Gruening, E.: Tr. Am. Ophth. Soc., 13:108-111 (Part I) 1912.

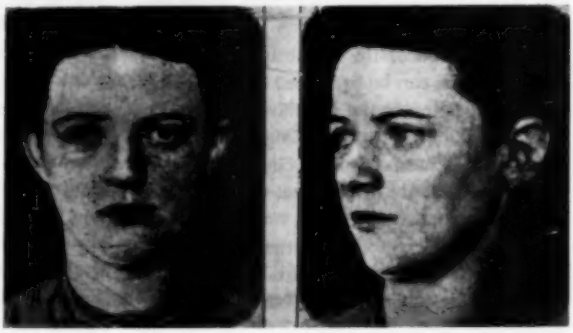


Fig. 2 (Doherty). Ten days after operation on January 26, 1912, the patient's appearance was practically normal.

There was an exophthalmos of 15 mm. in the direction of the orbital axis; the ocular conjunctiva below was chemotic, overlapping the lower lid, assuming a sausagelike roll over its entire length. The upper half of the bulbar conjunctiva was not involved. The motility of the eyeball did not exceed two mm. in any direction and was completely obliterated below. The media were clear, but the

optic nerve presented a choked disc of 6.0 D. elevation. Vision was 1/10. There was an ecchymosis of the lower lid from the onset of the attack, which remained stationary during the period of observation of six weeks. The girl was perfectly healthy; she had received no injury; there was no history of hemophilia in the family.

She was admitted to the hospital on January 15, 1912, and X-ray examinations of the sinuses and orbit were negative, as was a clinical exploration of the nose and sinuses. The Wassermann and Von Pirquet tests were both negative.

The treatment from January 15 to January 26, 1912, consisted of large doses of potassium iodide and cold compresses. She had no pain or fever but there was no diminution of the exophthalmos. Since there was no pulsation or susurrous in the orbital tumor, in view of the youth of the patient, a diagnosis of a rapidly growing orbital sarcoma was made and operative interference was decided upon.

On January 26, 1912, Dr. Gruening made a skin incision for the Krönlein operation with a view of resecting the outer wall of the orbit, if necessary. Next the orbital fascia was incised, and immediately a soft encapsulated mass protruded into the incision. It was not orbital fat, nor any structure that was usually found in the orbit.

The mass was incised and a large quantity of fluid blood was evacuated. When the sac was emptied the hemorrhage ceased, proving that an

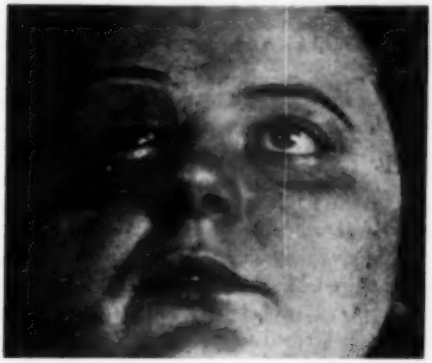


Fig. 3 (Doherty). Appearance of the eye at the time of the second attack, 12 years later in March, 1923.

incision had not been made into a sac connected with an open vessel.

Because of the high degree of exophthalmos, 15 mm., Dr. Gruening states that it was easy to explore the whole orbital cavity, and relates the difficulty experienced in such an examination in lower degrees of exophthalmos even after resection of the external bony wall.

The eyeball receded, the cutaneous wound was closed, and 10 days after the operation the patient's appearance was practically normal (fig. 2). The optic neuritis disappeared, she regained her sight, with limitations of motion fully restored in all directions except downward.

In concluding his report of this case, Dr. Gruening quotes from Adami who wrote in his *Principles of Pathology:* "The extensive hemor-

Fig. 4 (Doherty). Three months after treatment in 1923.

rhages into the substances of sundry organs may result, not in the ultimate absorption of the exuded fluid, but in cyst formation. The hemorrhage leads to the destruction of the tissues of the infiltrated area and eventually a capsule is formed around the exuded blood."

Dr. Gruening thought that this process had occurred in his case and believed that ecchymosis of the lower lid, as occurred in this case, was of diagnostic value. He states, in Merkel's *Anatomy of the Orbit,* that the septum orbitale forms a strong and firm barrier above and at either side. Below, however, it is perceptively thinner, and particles of orbital fat at times force their way through it.

According to Dr. Gruening, the likelihood is that, in this hemorrhage in the cellular orbital tissue, some blood followed the path of least resistance and appeared under the skin of the lower lid. As such persistent ecchymosis in the lower lid does not occur in other forms of tumor of the orbit, it may be considered pathognomonic of certain forms of spontaneous orbital hemorrhage.

Second attack

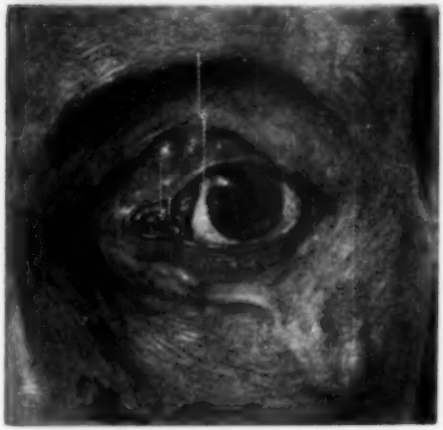
Twelve years later, in March, 1923, this same patient suffered a similar episode. She was admitted to Bellevue Hospital. At this time the picture (fig. 3) and findings were almost identical to those which existed in 1911 when she was 17 years of age.

There was marked ecchymosis and swelling of the lids, intense ecchymosis of the conjunctiva, and at least four mm. of exophthalmos with slight haziness of the cornea. The vision was reduced to counting fingers at about 10 feet.

The principal treatment at Bellevue Hospital in 1923 consisted of cold compresses and pressure bandages. After three months, the swelling subsided (fig. 4). There was a slight limitation of motion toward the nasal side and a partial symblepharon was present in the lower lid. A marked evidence of a hemangioma in the lower lid manifested itself

by simulating a bag of bluish earthworms which seemed to shine through the skin. The entire mass could be definitely palpated by the fingers and seemed to consist of a bundle of blood vessels. These vessels did not pulsate.

The patient was given a series of treatments with X ray and radium, and there was a gradual diminution of the evidences of the tumor. Upon



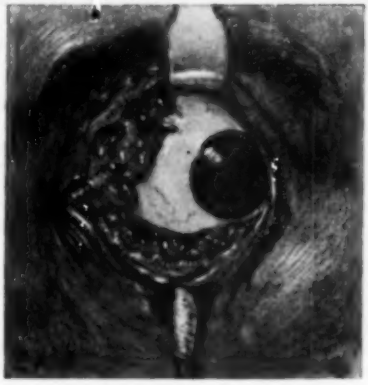


Fig. 5. (Doherty). Simple hemangioma.

leaving Bellevue Hospital, corrected vision was: R.E., 20/50; L.E., 20/20.

The fundus of the right eye showed an area of choroidal atrophy which manifested itself as a series of radiating streaks starting about two disc diameters from the disc on the nasal side and proceeding in a downward direction, giving the impression of having been caused by a rumpling of the eyeball itself due to the pressure of the tumor.

The fields presented a concentric contraction of about 15 degrees; the disc was pale and atrophic. X-ray films of the orbit and the Wassermann reaction were negative. The left eye, with the exception of an error of refraction, showed no pathologic condition.

THIRD ATTACK

On July 14, 1938, this patient had a third attack of exophthalmos which appeared, clinically, to resemble the second attack. However, the proptosis was two mm. with slight displacement up and to the right and some limitation of motion to the nasal side.

The mass, which could be palpated and which had previously simulated a bag of earthworms, now seemed more superficial and of a solid consistency and encapsulated. The vision and error of refraction had not changed. This is interesting in view of the severe trauma to which the eyeball had been subjected. Operative interference was decided upon on a number of occasions but, because the exophthalmos cleared, this procedure was abandoned.

My last examination of this patient (now aged 54 years) was on October 8, 1948. There were faint scars on the skin of the face, the after result of the first operation. There was no exophthalmos, and the motility was good in all directions. The marked symblepharon which was produced by the trauma of the second attack remains, and is a source of considerable annoyance because it partially obliterates the lacrimal puncta, producing considerable epiphora. There is a slight divergence, but this condition is not due to any ocular paresis but exists because of the poor vision which is 5/200; this diminution of vision is caused by an incipient posterior cortical cataract and partial optic atrophy. There is only a slight suggestion of the streaks which resembled folds in the choroid and retina.

This case is unusual. At the first attack, there was sudden rupture of a hemangioma, which gave no evidence of its existence until it ruptured. The second and third attacks were in all probability caused by thrombi which, it seemed to me, tended to eradicate the growth by, in a sense, ligating the vessels. The X-ray report taken at the New York Eye and Ear Infirmary during the third attack follows:

No pathologic changes were apparent in the radiographs of the right orbit. There were no evidences of bone destruction or hyperostosis, and no tumor masses could be discerned. There were no intracranial calcifications. No pathologic changes were apparent in the base of the skull, including the

sella. The sinuses showed no evidences of pathologic processes.

150 West 55th Street (19).

NOTE. Although I am unable to give a complete record, I should like to add the following case to ophthalmic literature. A patient was admitted on the service of the late Dr. Robert G. Reese, at the New York Eye and Ear Infirmary, in 1916, with a tumor which should be classified as a simple hemangioma with no capsule. Electrolysis and the attempt to ligate the main vessels failed to effect a cure for collateral circulation was established.

References

1. Benedict, W. L.: Diagnosis of orbital tumors. J.A.M.A., **126**:880-884 (Dec.) 1944.
2. ———: Surgical treatment of tumors and cysts of the orbit. Am. J. Ophth., **32**:763-773 (June, Part I) 1949.
3. Berens, C.: The Eye and Its Diseases. Philadelphia, Saunders, 1936.
4. Doherty, W. B.: Some of the most important ocular and orbital wounds in war. Am. J. Ophth., **25**:135-149 (Feb.) 1942.
5. Gruening, E.: Idiopathic hematoma of the orbit. Tr. Am. Ophth. Soc., **13**:108-111 (Part I) 1912.
6. Love, J. G., and Benedict, W. L.: Transcranial removal of intraorbital tumors, J.A.M.A., **129**: 777-784 (Nov.) 1945.
7. Reese, A. B.: Orbital tumors and their surgical treatment. Am. J. Ophth., **24**:386 (Apr.) 1941.
8. Renard, G., and Offret, G.: Arch. d'opht., **6**:284-313, 1946.
9. Stallard, H. B.: A plea for lateral orbitotomy (Krönlein's operation). Brit. M. J., March 29, 1947, pp. 408-409.

PRIMARY TUBERCULOSIS OF THE CONJUNCTIVA*

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Chicago, Illinois

The infrequency of primary tuberculosis of the conjunctiva in this country and the absence of any mention in the literature of treatment of this condition with streptomycin have prompted the present report.

Although Arlt[1] first described tuberculous infection of the conjunctiva in 1864 and Eyre[2] was able to collect 429 probable cases from the literature by 1912, only isolated instances have been reported in this country (Cohen,[3] Coover,[4] McKenzie,[5] Sitchevska and Sedam,[6] Thompson,[7] Goldfarb and Seltzer.[8]

Bruce and Locatcher-Khorazo[9] remarked "primary tuberculosis of the conjunctiva is rarely seen in this country. Bordley[10] was unable to find a case among over 41,000 patients treated at the Baltimore Eye, Ear, and Throat Charity Hospital. E. Burchell[11] could not recall having seen the disease in his 20 years at the New York Eye and Ear Infirmary, and we have found no mention of it among the records of the Institute of Ophthalmology in New York."

Treatment has hitherto consisted of radical excision, local ultraviolet light, X-ray therapy, iodoform powder, bland irrigations, and so forth, and has generally produced uncertain results. Tuberculin has not usually given good results in conjunctival lesions (Duke-Elder[12]).

Report of a case

Mrs. M. L., 27-year-old white woman, was first seen in the Central Free Dispensary of the Presbyterian Hospital on March 1, 1947. At that time she complained of redness, foreign-body sensations, and purulent discharge from the left eye of two weeks' duration. For approximately the same period she had experienced pain in the angle of the jaw on the left. Past history revealed that the patient had given birth to an eight-month premature stillborn infant in August, 1946. Past history was otherwise negative.

* Presented before the Chicago Ophthalmological Society, March, 1949. From the Presbyterian Hospital.

Family history was noncontributory. There was no known exposure to tularemia, lues, tuberculosis, or other infection.

Physical examination. The patient was well developed and well nourished. She did not appear ill and was alert and coöperative. The temperature was 99°F., the pulse rate, 80; the respiratory rate, 20; and the blood pressure, 120 mm. Hg (systolic) and 68 mm. Hg (diastolic).

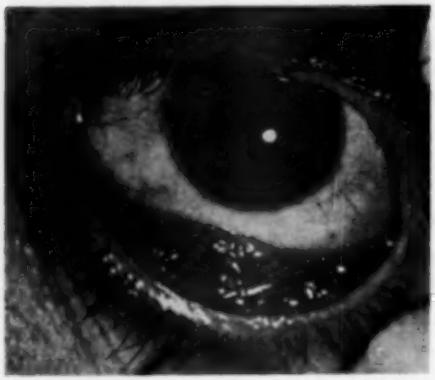

Fig. 1 (Donegan). Appearance of conjunctiva of left lower lid on April 8, 1947, showing marked follicular hypertrophy.

Ocular examination showed a slight redness and thickening of the left lower lid and a marked degree of injection and hypertrophy of the left caruncle and semilunar fold. An intense redness and follicular hypertrophy of the conjunctiva of the left lower lid was present and the lower fornix conjunctiva showed an irregular 4 by 6 mm. horizontally oval area of gray-white adherent necrotic tissue. The left preauricular gland was palpably enlarged and somewhat tender.

Within the next several weeks the entire conjunctiva of the left lower lid became more markedly injected and hypertrophied and thrown into ridgelike folds (fig. 1). The area of necrosis spread laterally to measure 11 by 3 mm. and the left preauricular gland increased in size (fig. 2). Vision in each eye was 1.0 and the remainder of the ocular examination was completely negative.

The differential diagnosis was held to lie among the following: (1) Parinaud's oculoglandular syndrome, (2) ocular glandular tularemia, (3) tuberculosis of the conjunctiva, (4) diphtheritic membranous conjunctivitis, and (5) chancre.

Laboratory examinations. The hemoglobin concentration was 14 gm.; the red cell count, 4,250,000; and the white cell count, 7,600. The urinalysis was negative and sterile catheterized specimens of urine revealed no organisms on smear and no growth on culture.

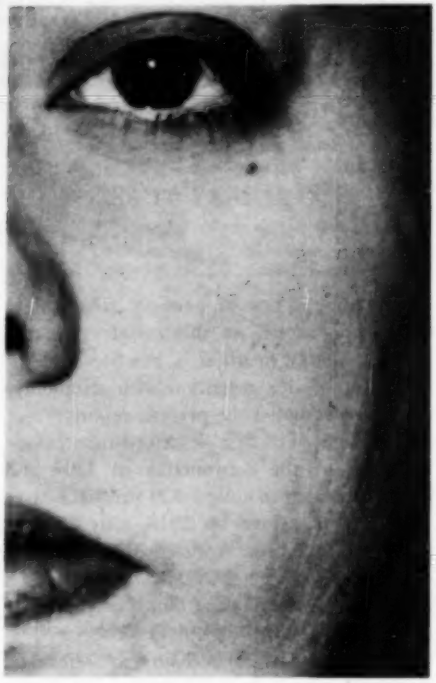

Fig. 2 (Donegan). Swelling of left pre-auricular gland as observed six weeks after onset.

Agglutination tests were negative for Eberthella typhosus, Salmonella paratyphoid A and B, proteus ×19, Brucella abortus, and Rickettsia prowazeki. Blood Kahn and Wassermann tests were negative as was a dark field examination.

Tests with old tuberculin in dilutions of 1:10,000 gave a positive reaction in 48 hours; the area of erythema extended 7 by 8 cm.

Repeated roentgenograms of the chest, left mandible, long bones, lumbar spine, pelvis, abdomen, and kidneys revealed no abnormalities. No stone shadows were present in the region of the left parotid.

Bacteriologic examinations. Smears, scrapings, and cultures were repeatedly obtained. Giemsa and Gram stains revealed no organisms. The Tiehl-Nielsen method was several times reported as negative but five weeks after the patient was first examined several acid-fast bacilli were observed. Cultivation on Loeffler's, Sabouraud's, brain broth, blood agar, dextrose broth, and Frobisher's egg media originally revealed only Streptococcus viridans but on April 5, 1947, several pure cultures of Mycobacterium tuberculosis were obtained from the inoculated egg medium. Guinea-pig inoculations from conjunctival scrapings and material aspirated from the preauricular gland produced typical tuberculous lesions.

Fig. 3 (Donegan). Photomicrograph of biopsy specimen. Granuloma contained giant cells and epithelial cells.

Pathologic study. On April 7, 1947, a biopsy was obtained from the necrotic area of fornix conjunctiva. The pathologic report was as follows:

Fig. 4 (Donegan). Conjunctiva of the left lower lid presented only slight injection and a few follicles after 17 days of streptomycin therapy.

Gross. The gross specimen consists of one piece of tissue, formalin-fixed, labelled "biopsy of left conjunctiva." The specimen is gray in color with fine pink lines over the surface. It measures 5 by 3 mm. The entire specimen is used for microscopic study.

Histology (fig. 3). In this section there is a granuloma containing giant cells and epithelial cells. This reaction is characteristic of tuberculosis. There is considerable chronic inflammation.

Diagnosis. Tuberculosis of conjunctiva.

Treatment and course. During the first four weeks after admission, treatment consisted of penicillin ointment (1,000 units per gm. instilled in the conjunctival sac every three hours) and hot compresses three times daily. After the first week, 30 minims of saturated solution of potassium iodide was ingested daily. Throughout this period there was no improvement in the inflammatory reactions in the palpebral conjunctiva, and the necrotic area in the lower fornix conjunctiva increased slowly in size as did the left preauricular gland. After several weeks the left submaxillary gland also became swollen and indurated.

Following the positive culture and biopsy report, the patient was admitted to the Presbyterian Hospital and for 17 days received

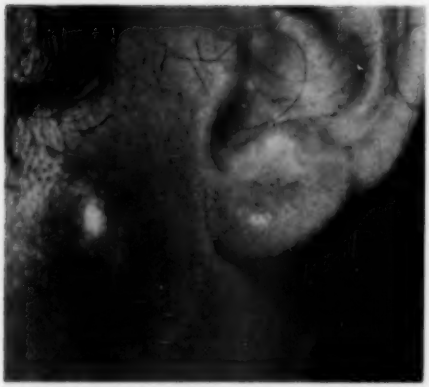

Fig. 5 (Donegan). Appearance of the left preauricular gland on June 27, 1947.

parenterally 125,000 units of streptomycin every three hours (one gm. daily). At the end of this period the necrotic area in the conjunctiva of the lower fornix had completely resolved and only a few follicles and mild injection remained (fig. 4). On the 14th day of hospitalization, the patient received one treatment of superficial X-rays directed to the left preauricular gland. Four days later a similar X-ray treatment was given. In view of the almost complete resolution of the conjunctival lesion, the streptomycin was discontinued and the patient was discharged from the hospital 17 days after admission. At this time pelvic examination revealed an early intra-uterine pregnancy.

Resolution of the adenopathy was considerably slower. After the second X-ray treatment, the preauricular mass became fluctuant and on June 3, 1947, yellowish purulent material was aspirated from the area. This procedure was repeated on June 16th, and June 23rd. During the first three weeks of June, three X-ray treatments were given (fig. 5). However no improvement was apparent and on July 2nd, she was again admitted to the hospital and 125,00 units of streptomycin every three hours were administered for the succeeding 21 days. The left preauricular and submaxillary swelling subsided slowly, the latter completely disappearing by October, 1947.

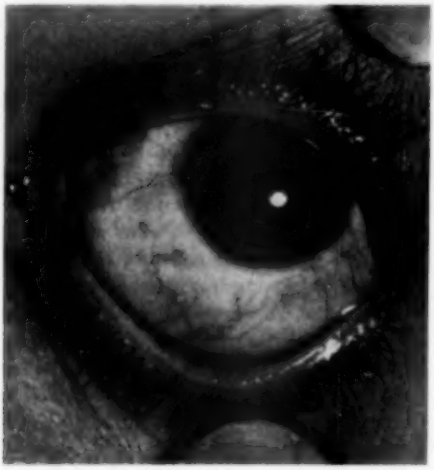

Fig. 6 (Donegan). Left lower palpebral conjunctiva appeared essentially normal on January 20, 1948.

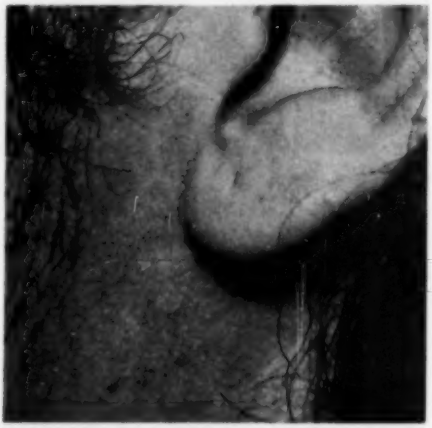

Fig. 7 (Donegan). Only a flat 2 by 3 cm. area of induration remained at the site of the left preauricular adenopathy on January 20, 1948.

On December 4, 1947, the patient had a normal spontaneous delivery of a full-term healthy male infant. One year after admission, the left lower lid and fornix conjunctiva were completely normal except for slight injection and follicular roughening. There

was no tenderness and only a flat 3 by 2 cm. area of induration in the region of the preauricular gland (figs. 6 and 7). When last examined on March 7, 1949, the conjunctiva was entirely normal and only a slight reddish discoloration of the skin was evident in the preauricular gland area. General health had been excellent and physical examination and chest X-ray studies done at this time were entirely negative.

SUMMARY

A case of primary tuberculosis of the conjunctiva, proved by bacteriologic and histologic methods, is presented. Treatment with streptomycin appeared to be of definite value in promoting recovery of the conjunctival lesion and to a lesser degree of the preauricular adenopathy.

122 South Michigan Avenue (3).

REFERENCES

1. Arlt: Klin. Monatsbl. f. Augenh., **11**:30, 1864.
2. Eyre: Lancet, **1**:1319, 1912.
3. Cohen, M.: Tuberculosis of the conjunctiva. Arch. Ophth., **48**:96, 1919.
4. Coover, D.: Tuberculosis of the conjunctiva. Am. J. Ophth., **3**:206, 1920.
5. McKenzie, W.: Tuberculosis of the conjunctiva. Am. J. Ophth., **22**:744, 1939.
6. Sitchevska, O., and Sedam, M.: Primary tuberculosis of the conjunctiva. Arch. Ophth., **30**:196 (Aug.) 1943.
7. Thompson, J.: Report of a case of primary tuberculosis of the conjunctiva. Ann. Ophth., **15**:76, 1906.
8. Goldfarb, A. A., and Seltzer, I.: Primary tuberculosis of the conjunctiva. Am. J. Dis. Child., **72**: 211-215 (Aug.) 1946.
9. Bruce, G. M., and Locatcher-Khorazo, D.: Primary tuberculosis of the conjunctiva. Arch. Ophth., **37**:375, 1947.
10. Bordley, J.: Tuberculosis of the conjunctiva. Ophth. Rec., **11**:368, 1902.
11. Burchell, E.: Cited by Sitchevska and Sedam.[6]
12. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, Mosby, 1938, v. 2, p. 1636.

A CASE OF BILATERAL STURGE-WEBER SYNDROME*

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The nevus flammeus (port-wine nevus) of the face is a striking feature that attracts the interest not only of a general practitioner. Its frequent association with glaucoma has been known for almost 90 years (Schirmer, 1860) and yet there are only about 150 cases reported in literature. We are dealing, therefore, with a rare disease and the report of another typical case is worthwhile, particularly if it presents the interesting behavior of the intraocular pressure after the massage test, as was observed in our case.

CASE REPORT

Our patient, a boy, aged two years, was first admitted to the hospital when five months old for repeated attacks of convulsions. An outline of the patient's hospital record† shows:

The family history is essentially negative. There is no frequent occurrence of nevi. A brother and a sister of the mother are suffering from schizophrenia. Two brothers and a sister of the patient are normal. The mother was healthy during the pregnancy and delivered normally at full term.

The baby appeared healthy and well developed but the big hemangioma of the face and the forehead was noticed right after birth. The hemangioma was irradiated (X-

* From the University Eye Clinic of Geneva: Director, Prof. A. Franceschetti, and the Children's Hospital, Aarau: Director, Dr. T. Baumann.

† I wish to thank Prof. H. Willi, director of the baby nursery of the Kantonale Frauenklinik in Zürich who kindly provided the clinical records of this case.

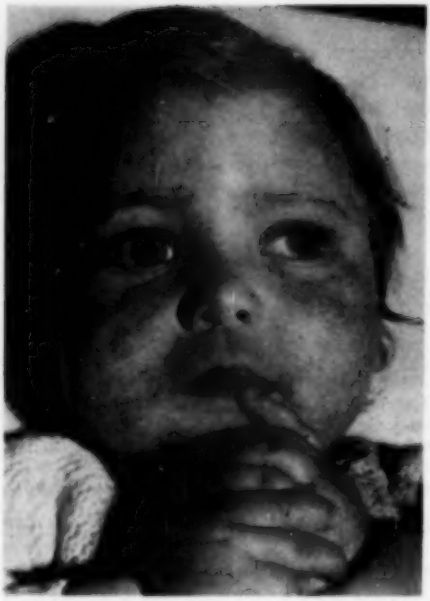

Fig. 1 (Bock). The bilateral nevus flammeus corresponded to the skin area innervated by the second and third branches of the trigeminus.

rays) 3 and 4 months later. Soon after the second irradiation, the baby became apathetic and developed tonic clonic convulsions, mainly of the whole left side, lasting about two hours. There was no fever. Similar convulsions occurred every 3 to 4 days, usually left-sided, occasionally also on the right side.

On admission to the hospital, the general examination showed a big, strong baby, with a normally developed physique, but mentally apathetic. The child did not follow moving objects with the eyes. The skin was generally puffy and there was a large bilateral hemangioma over the upper lip, cheeks, eyelids and forehead, extending backward beyond the coronal suture, leaving untouched only a vertical streak of the forehead and a small white spot on the left side of the tip of the nose. It corresponded in extension to the skin areas innervated by the first and second branches of the trigeminus on both sides. Its color was deep red and there were many fine telangiectases on the right side.

There was another small hemangioma over the left lower leg and a pigment nevus on the right thigh. The large fontanelle was depressed. The eyes showed an enlarged cornea on the right side only, the discs were of normal color with a "physiologic" cupping. The tension was normal by palpation. Except for a marked lymphocytosis (60 percent), all other findings, including neurologic examination, were normal.

The convulsive attacks—usually localized on the left side—recurred a few times until an encephalography was made which improved the general condition and stopped the convulsions. The spinal fluid, obtained during the air filling, was under normal pressure, showed an increase in protein contents (mainly the albumin fraction) of 66 mg. percent, and a normal goldsol curve. The X-ray film showed an atrophic process on the surface of the right hemisphere; the lateral ventricles were normal.

X-ray irradiations of the right side of the head were given again every six weeks without any incident. The child developed well physically but showed marked mental retardation.

At the age of 11 months the left-sided convulsive attacks recurred, this time complicated by vomiting and temperature. The spinal fluid was under a pressure of 20 mm. of water, proteins were increased to 170 mg. percent, and it presented a meningitic goldsol curve. The whole picture was explained as a reaction to the X-ray treatment which, therefore, was discontinued.

An eye examination at this time showed enlarged corneas (12 to 13 mm.) on both sides, telangiectases of the conjunctiva, slight temporal pallor of both discs, and some tortuous retinal vessels. Tension by palpation was normal.

The child was not bothered any more by the attacks till he reached his 23rd month. He was admitted to the Children's Hospital, Aarau, with temperature, vomiting, stomatitis, unconsciousness, and convulsions be-

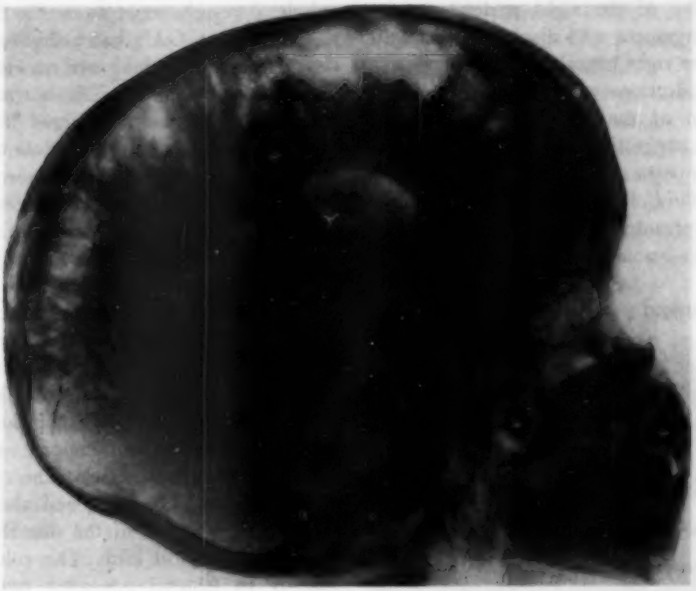

Fig. 2 (Bock). Lateral view of the skull after air filling. There was marked atrophy of the gyri mainly in the parietal region, with suggestive erosion of the inner lamina compacta.

ginning on the left side, spreading to both sides, and lasting for almost two days.

Dr. T. Baumann obtained the following findings:

Examination showed a big, overweight child, apathetic, idiotic, with marked muscular hypotony. He could lift his head, but was unable to sit up. There was a nevus flammeus of the same distribution as has been described (fig. 1). Its color was not as bright as it was a year previously (? X-ray treatment). Internal organs were normal. Patellar reflexes were exaggerated and equal on both sides; otherwise, the neurologic findings were normal.

X-ray studies of skeleton. No calcification centers in the carpal bones (developmental retardation). Large fontanelle closed.

Encephalography (figs. 2 and 3). Exten-

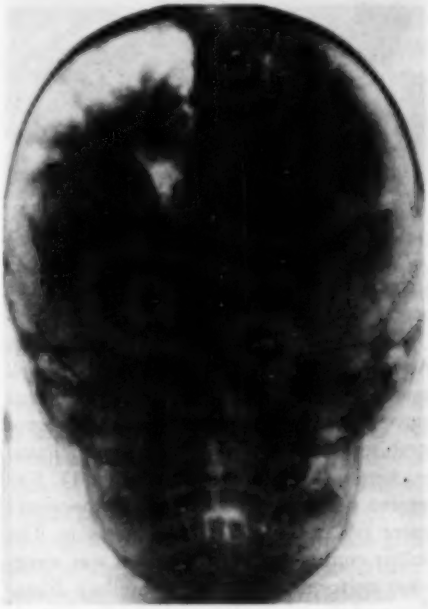

Fig. 3 (Bock). A front-view encephalogram, showing atrophy of the cortex of the right side and displacement and slight enlargement of the right lateral ventricle.

sive atrophy of the right parietal cortex; slight enlargement and displacement to the right of the right lateral ventricle.

No calcifications were seen on the plain X-ray film of the skull but there was a region of suggestive erosion of the inner lamina compacta of the parietal bone.

Spinal fluid. Pressure normal. Proteins: 160 mg. percent; 18/3 cells; goldsol curve pointing to an involvement of the parenchyma.

The marked muscular hypotony with

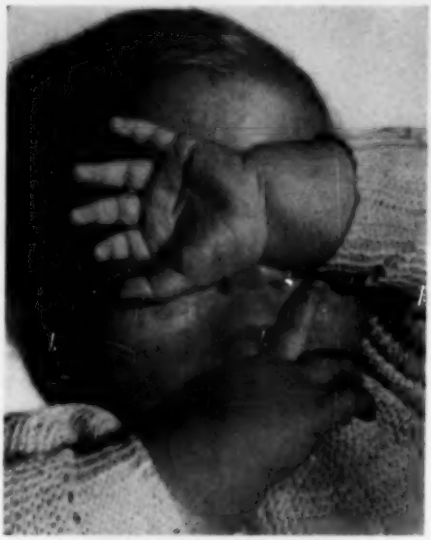

Fig. 4 (Bock). The digito-ocular sign of Franceschetti.

atrophy of the cortex is an unusual feature here.

The ocular findings were the following: Apparent blindness of both eyes which look usually to the right side with occasional movements in other directions (divergent strabismus). The digito-ocular sign of Franceschetti (1947) was positive (fig. 4). Extensive nevus flammeus of both upper and lower lids, more red on the right side. The bulbar conjunctiva on both sides was somewhat uniformly pink due to capillary dilatation and there are also several telangiectatic episcleral vessels, more so on the right side.

The corneas, O.U., had a shining surface, clear stroma, and there are no ruptures in Descemet's membrane. The horizontal and vertical diameters are enlarged to 13 mm. The anterior chamber was of about normal depth. The irides were blue, of normal structure, O.U. There was no heterochromia.

Several strands of persistent pupillary membrane were found across the right pupil. The pupils reacted rather well to light directly and consensually but not as promptly as is customary in a child of this age. Lens and vitreous were clear.

The fundi showed an atrophic white excavated disc; that on the right side showed a more extensive total cupping and nasal displacement of the vessels. The excavation amounted to 5.0D., O.D., and about 3.0D., O.S. On the border of the disc the vessels showed the typical kink. The color of the fundus in general appeared redder than usual but it was difficult to tell whether this was not due to the contrast with the pallor of the atrophic disc.

The retinal vessels were normal except for the nasal upper vein, O.D., which was very tortuous and spiraled several times around the normal nasal upper artery. The macula was normal, O.U.

The pigment epithelium was rather dense so that no details of the choroid, not even in the periphery, could be seen.

Refraction (by direct ophthalmoscopy). Emmetropia, O.U.

Tension. 20 to 22 mm. Hg (Schiøtz), O.U., on several occasions. The behavior of the intraocular pressure after homatropine and after the massage test (Knapp, 1912) was interesting. Homatropine, which had been given as a routine procedure for fundus examination, hardly raised the pressure (26 to 28 mm. Hg). Massage of the eyeball for one minute was performed on a later occasion.

According to investigations of P. Knapp, this should be followed in a normal eye by a lowering of the tension to one half or even

one third of its original value; the tension then rises again slowly to normal level at the end of one hour; in glaucoma with predominantly insufficient drainage, it drops only slightly or not at all and returns rapidly to normal or higher level. This simple massage test was the only one considered safe enough to be tried in this child.

Originally, it was intended to investigate (1) the drainage system by this test and (2) to observe the influence of vascular dilatation (? angioma of the choroid) on the intraocular pressure by giving vasodilators (amyl-nitrite inhalation or Priscol as retrobulbar injection). However, in view of the fact that our patient had an extensive cerebral lesion, most likely also of angiomatous nature, with attacks of convulsions, the latter procedures were omitted. We hope that these tests will be used safely in patients who do not present such an extensive pathologic picture.

The results of the massage test were striking: The tension did not drop at all after one minute of deep massage of both eyes and rose rather rapidly to 38 mm. Hg, O.D., and 34 mm. Hg, O.S. in less than half an hour after massage ended. There was no appreciable change in the depth of the anterior chamber before and after massage.

It must be stated that tonometry was relatively easy in our little patient and the readings, therefore, are reliable, which is probably not always the case in a child of this age.

Discussion

We are dealing here with a case of Sturge-Weber-Krabbe syndrome. It shows the full symptomatology of nevus flammeus of the face (here bilateral), a unilateral meningeal (? cerebral: Krabbe, 1934) lesion of probably similar nature causing mental retardation with epileptiform attacks, and, finally, a bilateral hydrophthalmos.

The bilateral occurrence of the nevus and the hydrophthalmos is unusual but such cases have been reported, particularly when the nevus was widespread (Beltmann, 1904; Horay, 1929; Knapp, 1928; Koyama, Ayao, 1937; Marchesani, 1925; Rodigina, 1944; Safar, 1923; Vagts, 1937).

In our case, in spite of the bilateral distribution of the vascular lesions, there is a definite unilateral tendency. The cerebral lesion is—at least as far as the X-ray film shows—unilateral and on the same side where the nevus is more extensive and where the glaucoma is more advanced (cupping deeper, O.D., than O.S.).

The involvement of the conjunctiva by the vascular anomaly is not too frequent (Bär, 1925; Blum, 1949; Ginzburg, 1926; Komoto, 1922; Rötth, 1929). In our case, it is also more marked on the right side. The strands of persistent pupillary membrane and the very tortuous retinal vein are all on this side. As in most cases reported in literature, our case shows no tears in Descemet's membrane in spite of the enlargement of the cornea. Franceschetti's (1937) case seems to have been a rare exception.

Of particular interest is the behavior of the intraocular pressure in our case. First, its values were normal under ordinary conditions and then it reacted to the massage test as has been described, which indicates a great lability (see Beauvieux and Bessière's case, 1944). Previous periods of raised tension seem to be responsible for the cupping and atrophy of the discs.

The apparent complete blindness with persistent pupillary reaction to light is also an unusual feature. It makes one think that an intracranial (cortical) lesion might play a rôle in addition to the glaucomatous optic atrophy.

Although there is almost universal agreement that this syndrome has to be considered as a congenital anomaly belonging to the group of van der Hoeve's (1936) phacomatoses (tuberous sclerosis, von Hippel-Lindau's disease, neurofibromatosis of von Recklinghausen), the etiology of the glaucoma in these cases is not well understood. More than likely, it is directly related to the vascular anomaly, a view supported by the

frequent finding of uveal angiomas (Stoewer, 1908; Ballantyne, 1940; De Haas, 1929; Galezewski, 1898; Knapp, 1928; Lawford, 1885; Jahnke, 1931; Milles, 1884; O'Brien and Porter, 1933; Patton and Collins, 1919; Tyson, 1932), dilated choroidal vessels (Salus, 1923), telangiectases and tortuosity of vessels (Clausen, 1928; Davies, 1939; Elschnig, 1918; Horrocks, 1883; Krause, 1929; Rosen, 1944; Snell, 1886; Sturge, 1879), and a generally brighter red color of the fundus (Yamanaka, 1927).

This "plethoric glaucoma" theory (Elschnig) has something convincing, particularly if we also remember the case of Zaun (1924) which showed a rise of intraocular pressure manifested by corneal edema every time the homolateral facial nevus became red by an irritation.

Also, histologic study has shown in several of the examined cases (Snell, 1886; Milles, 1884; De Haas, 1929; Jahnke, 1931; Stoewer, 1908) an angioma of the choroid, and all cases showed intraocular capillary dilatation (Duke-Elder) which could be the important factor in the development of glaucoma.

On the other hand, deficient drainage was assumed as the primary cause of the glaucoma on the basis of histologic examination in which only or mainly an anomaly of the Schlemm canal could be found (Safar, 1923; Vagts, 1937). This anomaly was of the same type as the one usually found in cases with ordinary hydrophthalmos without nevus flammeus and described by Seefelder (1906) and Reis (1905).

It seems most likely that both factors—vascular and drainage anomalies—are always simultaneously effective in producing the glaucoma, the one or the other predominating in different cases.

In our little patient's case, the reaction to the massage test would support very convincingly this point of view. There certainly is a deficient drainage and there must be at the same time quite a marked vascular (capillary) anomaly to explain the unusual rise in tension in the space of half an hour.

Summary

A case presenting the full symptomatology of bilateral Sturge-Weber syndrome is reported. The interesting behavior of the intraocular pressure after the massage test makes one assume that the etiology of the glaucoma in this case—and may be in all cases—is due to an anomaly of both the drainage and the choroidal vascular bed.

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References

Ballantyne, A. J.: Brit. J. Ophth., **24**:65, 1940.
Beltmann, J.: Arch. f. Ophth., **59**:502, 1904.
Bär, C.: Ztschr. f. Augenh., **57**:628, 1925.
Beauvieux, J., and Bessière, E.: J. de méd. Bordeaux, 1944, No. 1-2, p. 21. (From Larmande, A. M.)
Blum, J. D.: Ophthalmologica, **118**:781, 1949.
Clausen: Discussion of Voegele: Abstract, Klin. Monatsbl. f. Augenh., **81**:393, 1928.
Cordero, C.: Atti Soc. opht. ital., **8**:267, 1943.
Davies, W. S.: Am. J. Ophth., **22**:298, 1939.
Duke-Elder, W. S.: Textbook of Ophthalmology. London, Kimpton, 1941, v. 3, pp. 3322-3323.
Elschnig: Ztschr. f. Augenh., **39**:189, 1918.
Franceschetti, A.: Ophthalmologica, **114**:332, 1947.
Franceschetti, A., and de Morsier, G.: Schweiz. med. Wchnschr., **67**:485, 1937.
Galezowski, M.: Ann. de dermat. et syph., **9**:245, 1898.
Ginzburg, J.: Klin. Monatsbl. f. Augenh., **76**:393, 1926.
De Haas: Abstract, Zentralbl. f. d. ges. Ophth., **20**:847, 1929.
Van der Hoeve, J.: Deutsche Ophth. Ges. Heidelberg, 1936. Abs.: Zentralbl. f. Ophth., **36**:325, 1936.
Horay, G.: Zentralbl. f. Ophth., **20**:793, 1929.
Horrocks, P.: Tr. Ophth. Soc. U. Kingdom, **3**:106, 1883.
Jahnke, W.: Ztschr. f. Augenh., **74**:165, 1931.
Knapp, A.: Arch. Ophth., **57**:219, 1928.
Knapp, P.: Klin. Monatsbl. f. Augenh., **1**:691, 1912.

Komoto: Klin. Monatsbl. f. Augenh., 69:158, 1922.
Koyama and Ayao: Chuo-Ganka Iho, 29:11, 1937.
Krabbe, K.: Arch. Neurol. & Psychiat., 32:737, 1934.
Krause, K.: Ztschr. f. Augenh., 68:224, 1929.
Larmande, A. M.: La neuro-angiomatose encéphalo-faciale. Paris, Masson, 1948.
Lawford, J. B.: Tr. Ophth. Soc. U. Kingdom, 5:136, 1885.
Marchesani: Wien. med. Wchnschr., 75:2538, 1925.
Milles, W. J.: Tr. Ophth. Soc. U. Kingdom, 4:168, 1884.
O'Brien, C. S., and Porter, W. S.: Arch. Ophth., 9:715, 1933.
Patton, L., and Collins, E. T.: Tr. Ophth. Soc. U. Kingdom, 39:157, 1919.
Reis, W.: Arch. f. Ophth., 60:1, 1905.
Rodigina, A. M.: Arch. Ophth., 32:214, 1944.
Rosen, E.: Am. J. Ophth., 27:1143, 1944.
Roetth, A.: Abstract, Zentralbl. f. d. ges. Ophth., 20:588, 1929.
Safar, K.: Zentralbl. f. Augenh., 51:201, 1923.
Salus, R.: Klin. Monatsbl. f. Augenh. 71:305, 1923.
Schirmer, R.: Arch. f. Ophth., 7:119, 1860.
Seefelder: Arch. f. Ophth., 63:430, 1906.
Snell, S.: Brit. J. Ophth., 2:68, 1886.
Stoewer, P.: Klin. Monatsbl. f. Augenh., 46:323, 1908.
Sturge, A.: Tr. Clin. Soc., 12:162, 1879.
Tyson, H. H.: Arch. Ophth., 8:365, 1932.
Vagts, E.: Dissertation, Kiel, 1937.
Weber, F. P.: Proc. Roy. Soc. Med., 22:25, 1929.
Yamanaka, T.: Klin. Monatsbl. f. Augenh., 78:372, 1927.
Zaun, W.: Klin. Monatsbl. f. Augenh., 72:57, 1924.

THE OCULAR MANIFESTATIONS OF RIBOFLAVIN DEFICIENCY*

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Ten years ago, Bessey and Wolbach[1] described and explained the corneal vascularization which occurs in rats maintained on a riboflavin-free diet. Shortly afterward Sydenstricker, Kruse, and their associates[2] published their observation of the same phenomenon in man. Unfortunately there is still some argument about its clinical significance. This is mainly caused by a faulty discrimination between normal and pathologic aspects of the vascular system of the limbus and the failure to recognize different types of true corneal vascularity. It is the purpose of this paper to review critically the different opinions and to compare them with my own experiences. Another and more important purpose is to present an explanation for the apparent incompatibility of findings regarding the ocular manifestations of riboflavin deficiency.

WHAT IS CORNEAL VASCULARITY?

Unmistakable corneal vascularity has been described by Bessey and Wolbach,[1] Sydenstricker and associates[2] and Kruse and associates.[3] Much trouble could have been avoided if Sydenstricker, Kruse, and their group had not included "conjunctivitis," "engorgement of the limbic plexus," and "circumcorneal injection" as early signs of ariboflavinosis, and if some of the subsequent workers had first made themselves familiar with the variations of the limbus as visualized by the slitlamp.

Corneal vascularity is a condition in which newly formed blood vessels leave the limbic plexus and centripetally enter the subepithelial space of the true cornea. This state, and nothing less, is acceptable as corneal vascularity.

The limbus is not a line but a band about one-mm. wide, consisting of the wedge-

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shaped edge of the sclera which overlaps the corneal tissue, the cornea being inserted into the sclera like a watch glass. The sclera bevels off from full thickness at the equatorial border to extreme thinness at the corneal edge. This area is plentifully provided with blood vessels which comprise the limbic plexus.[4]

The limbic plexus is not always visible in the living eye as the vessels frequently are empty, in which state they do not show. The plexus responds readily to mechanical or chemical irritation, which causes a conjunctival hyperemia and opens the vessels of the limbus. The state of filling of the limbic vessels may change from hour to hour, depending on light, wind, dust, accommodative strain, and so forth. They can be demonstrated clearly, according to their state of filling, with the aid of the slitlamp. The true cornea is usually sharply demarcated from the limbus, particularly when the light reflected from the iris is used, and normally is devoid of blood vessels.

Hyperemia of the limbic plexus, circumcorneal injection, and engorgement of the limbus have been regarded as early signs of ariboflavinosis. While this certainly may be the case, these signs are entirely nonspecific. The sprouting out of new vessels from the limbic plexus is preceded by engorgement and increased activity of the plexus itself. This condition will or will not respond to riboflavin administration, according to its etiology. For practical clinical purposes it must be insisted upon that new vessels must appear in the cornea before one can speak of corneal vascularity. The importance of a correct anatomic diagnosis has been emphasized before by Gregory,[5] Ferguson,[6] Mann,[7] Stern,[8] and others. It is stressed here again because much of the confusion regarding the causal relationship between riboflavin deficiency and corneal vascularity has been due to the various interpretations of the extent of "corneal invasion."

Let is be stated then once more that circumcorneal injection—that is, hyperemia of the blood vessels of the limbus—although it may represent the first stage of corneal vascularization, is a completely nonspecific response of the eye to any kind of irritation, or to an intraocular upset like iritis or glaucoma. It is entirely useless for the evaluation of an individual's state of nutrition with riboflavin.

Corneal vascularity itself is not always easy to detect. It requires considerable experience with the slitlamp to recognize the sometimes very fine and short capillaries which often can be seen only by indirect illumination in the light reflected from the iris.

The corneal vascularization of well-developed riboflavin deficiency always occurs in the entire circumference of the cornea. This fact is important for correct diagnosis. In view of the fact that riboflavin deficiency is nutritional and present throughout the organism, it is to be expected that both eyes show equally the resulting vascularity. This is the case in the great majority of patients. But there are exceptions to this rule. It will be shown later that disease or trauma may condition vascularization in one eye when the degree of riboflavin deficiency is insufficient to produce signs in the other eye.

Differential diagnosis of corneal vascularization

Invasion of the cornea by blood vessels occurs in several pathologic conditions of the eye. In rosacea keratitis it is usually accentuated in the upper quadrants of the cornea, but may also extend all around the limbus. This disease, however, is characterized by subepithelial infiltrates which increase in size and progress toward the center and the deeper layers of the stroma. Eventually the epithelium over these areas becomes eroded and the ensuing ulcers attract blood vessels which form a vascularization of the fascicular type.[9] This clinical picture is different from that of the ariboflavinotic type of corneal vascularity, and reports by Johnson and others[10] that rosacea keratitis responds to riboflavin therapy have been vigorously con-

tradicted by Fish,[11] Wise,[12] and others. It may be that a coincidental riboflavin deficiency can aggravate a rosacea keratitis, in which case some benefit may be derived from riboflavin administration.

Vascularization of the cornea also occurs in phlyctenular (eczematous) keratitis. In this condition the arrangement of the vessels is similar to that described in riboflavin deficiency. However, this fact presents no difficulties in the differential diagnosis. It has been shown by Landau and me[13] that phlyctenular keratitis is really a riboflavin deficiency conditioned by an allergic reaction. These cases respond so well to riboflavin medication that this alone should be proof enough for this contention. They display, in addition, low riboflavin excretion levels in the urine, and it can be categorically stated that phlyctenular or eczematous keratitis is a clinical variation of riboflavin deficiency in an allergic subject.

Another condition characterized by invasion of the cornea by blood vessels is trachoma. The trachomatous pannus is, of course, of an entirely different type, occupying only the upper half or third of the cornea. It cannot, therefore, be confounded with the ariboflavinotic vascularization. Landau and I[14] have shown that certain cases of clinically healed trachoma display a degree of activity of the pannus which is out of proportion to the conjunctival lesions. These cases show an additional corneal vascularity in the remainder of the circumference, and this condition responds readily to riboflavin administration. We take this as proof that this type of pannus is an exacerbation due to a riboflavin deficiency; the preformed channels of the originally collapsed, inactive pannus vessels are opened again when riboflavin deficiency causes the limbic plexus to throw out new vessels in the previously unaffected parts of the cornea.

These are the only known clinical conditions in which corneal vascularity more or less resembling that of riboflavin deficiency can be observed. As has been shown, the resemblance is only superficial in the case of rosacea keratitis, except possibly in some instances where the vascularity may be due to a primary riboflavin deficiency which prepared the cornea for an invasion by blood vessels in the presence of a conditioning factor.

Corneal vascularity of the same type as in riboflavin deficiency has been found to occur in rats on a diet deficient in one or more of the essential amino acids (tryptophane, leucine, phenylalanine, and so forth). Nothing much is known as yet of the pathogenic mechanism of this vascularization; it is probably due to some metabolic upset in the corneal cells caused by the absence of these substances. A similar type of vascularization occurs in zinc deficiency,[15] and sodium deficiency.[16] Although this vascularity is of the same type as that in ariboflavinosis, clinically it usually need not be taken into consideration in the differential diagnosis because it seems to occur only in experimental conditions which, it is believed, are unlikely to be encountered in clinical practice.

Specificity of corneal vascularization

It is necessary to discuss here critically the statement of a number of workers that corneal vascularity is not an unequivocal sign of riboflavin deficiency. Stannus,[17] in expressing this opinion, quotes several authors to whom he attributes statements to this effect. In checking the original papers one finds, in some instances, Stannus's interpretation of the authors quoted open to criticism; in other cases it seems likely that Stannus read into these papers a meaning which the authors never wished to express.

Goldsmith[18] looked, in a nutritional survey of patients in a charity hospital, for "vascularization of the cornea (grossly visible)" and "conjunctival congestion." She writes: "In a number of our patients injection of the conjunctival vessels appeared as a band extending across the bulbar conjunctiva from the xanthus to the limbus. . . ." This description and the expression "grossly visi-

ble" indicate that this author did not use a slitlamp, and what she describes is, of course, not corneal vascularity.

Kodicek and Yudkin[19] have made a survey of school children and considered in it encroachment of vessels upon the clear cornea as a sign of riboflavin deficiency; they write: ". . . Invasion of the cornea itself by capillaries from the limbus is more likely to be of definite dietary origin, and by considering only children showing this we think we are dealing with cases of real deficiency . . . the degree of vascularization which we have taken as abnormal is almost certainly due to riboflavin deficiency. . . ."

Keath-Lyle and others[20] say: "Vascularization of the cornea is not necessarily evidence of deficiency in the diet. . . . Riboflavin is not the only nutrient concerned in the prevention of corneal vascularization." However, these authors included hyperemia of the limbic plexus as corneal vascularity, and examined in their survey only "the nasal, inferior and temporal quadrant of both eyes . . ."—that is, they were not concerned with vascularization in the whole circumference. Moreover, they arrived at a score of vascularization by adding the number of corneal capillaries in each of the three quadrants observed, thus accepting cases of localized vascularity into their total number. It has already been pointed out that this is inadmissible.

Machella and McDonald's paper[21] concerns nine patients who failed to improve with riboflavin although they "showed the accepted picture of riboflavin deficiency." Two of their cases had chronic conjunctivitis without corneal vascularity, two others "vascularizing keratitis" which is not further described and may be anything, and five cases suffered from rosacea keratitis which does not respond to riboflavin.

Pett[22] failed to cure 43 percent of persons with corneal vascularity with riboflavin. His method, however, is objectionable; in his investigations "a record was made of the appearance of the limbus between 5 and 7 o'clock of the circle" and the rest of the cornea was disregarded.

Another authoritative paper quoted by Stannus is that by Tisdall, McCreary, and Pearce[23] who found a high prevalence of corneal vascularization in a group of healthy pilots of the Canadian Air Force; they reproduce excellent photographs of the cornea which, however, leave some doubt whether the actual cornea was invaded by blood vessels in all their cases, and it is not unlikely that they included some cases of limbic congestion. All the same they arrive at the following conclusions: "(1) The incidence of vascularization of the cornea among healthy young adults in Canada is surprisingly high and seems to vary with the riboflavin-containing foods in the diet. (2) Riboflavin in large dosage for a period of 2 months decreased the vascularity of the cornea in a large percentage of cases. . . ."

Their actual figures were: progressive decrease in the vascularity in 70 percent and clearing or improvement of symptoms in 95 percent. The administration of placebos in a control group caused no change in the vascularity. They found furthermore that the subjects under investigation were on an average daily intake of riboflavin of only 1.6 mg. It is not clear why Stannus quotes this excellent paper in support of his thesis that corneal vascularity is not always a sign of ariboflavinosis.

Finally, there is a paper by Youmans and others,[24] the result of a mass observation trying to define whether corneal vascularity may not be due to destruction of riboflavin by excessive light. The very object of this investigation indicates that the authors do not question the specificity of corneal vascularity, and in fact they say nowhere that it is not due always to riboflavin deficiency—be it local or systemic.

Scarborough[25] found circumcorneal injection in 34 percent of 204 cases, and in 68 percent of subjects over 50 years of age. He observes correctly that this condition is not caused by riboflavin deficiency, as ad-

ministration of riboflavin by mouth or parenterally did not influence it, and that a therapeutic test is the best criterion in establishing a diagnosis.

Scott[26] includes "circumcorneal vessels" and "invasion of the clear cornea with not more than one arcade" in his cases and it seems doubtful whether even the latter were true corneal vascularity. Wiehl and Kruse[27] investigated the problem within the framework of their work on nutrition and stated: ". . . but those with capillaries noted as having extended into the cornea in one or both eyes have been counted as cases of aribroflavinosis. . . ." It is obvious that they accept this as an unequivocal sign of ariboflavinosis and do not doubt its significance.

Sandstead[28] found 80 to 93 percent of vascularization of the cornea of children and young adults, but here again it is open to doubt whether he distinguished between true vascularity and circumcorneal congestion.

Stannus also mentions a paper by Wilson which I have been unable to find.

Those then are the workers on whose papers Stannus and others depend when they argue that corneal vascularity is not an unequivocal sign of ariboflavinosis. Who are the other workers taking the same attitude?

Anderson and Milam[29] doubt that milder degrees of corneal vascularity are due to riboflavin deficiency. The cases of corneal vascularity on which they base their opinion were, however, on an average daily intake of 0.5 to 1.3 mg. of riboflavin which is below the recommended daily allowance of 1.5 to 1.8 mg. It is doubtful, furthermore, whether these cases of "milder degrees" were not really only limbus congestion.

Boehrer and others[30] were unable to find corneal vascularity in six subjects who received 0.47 mg. of riboflavin daily for five weeks. This is too short a period of time to allow vascularization to make its appearance, and, in addition, the authors were not sure of the coöperation of their subjects.

McCreary, Nicholls, and Tisdall[31] make an important point which, however, does not disprove our thesis: they found that corneal vessels of ariboflavinosis never disappear entirely but become invisible when they are anemic and collapsed. They can refill at any time in response to a nonspecific irritation. This observation corresponds with that in trachomatous pannus, where the vessels persist as empty channels all through the life of a patient. This fact appears, therefore, to be a potential source of error. Even if it is agreed that corneal vascularity of the type discussed here is originally always due to riboflavin deficiency, a flare-up at a later stage may be caused by a nonspecific reaction to any kind of irritation. In this instance no response can be expected to riboflavin medication.

To summarize: there is no known clinical condition other than ariboflavinosis that produces the type of corneal vascularization seen in riboflavin deficiency. There are indications that the catalytic chain of respiratory processes in the cornea may occasionally break down at a different link—iron, amino acids, zinc—but it seems to happen most frequently at the riboflavin link.[32-36] The ariboflavinotic type of corneal vascularity is, therefore, not an absolutely pathognomonic sign of riboflavin deficiency, but unless a primary or secondary deficiency in these or related substances exists it is definitely indicative of a riboflavin deficiency and will respond to riboflavin. The therapeutic test provides the final answer.

It is necessary to mention here a paper which has caused me grave concern in the process of formulating the above conclusions. The findings of Borsook and others[37] in a survey of Californian aircraft workers are in direct opposition to the reasoning presented here. These workers found some degree of corneal vascularity in 100 percent of their subjects, and failed to observe any influence of riboflavin on this condition. In talking to one of the observers (E. A.), I was convinced that it was apparently true corneal vascularity which the authors had seen. This perturbing state of affairs is at

present entirely inexplicable to me. However, I am convinced that this unique paper must be based on some kind of misapprehension. No similar claim has been made by any of the other investigators on record, and to my mind it is inconceivable that every single individual of the 1,200 subjects of this survey should be an exception to the conclusions arrived at in the previous pages.

Does riboflavin deficiency always produce corneal vascularity?

The results of a survey in the Nutrition Clinic of the Health Department of New York City will be useful in the attempt to arrive at an answer to this question.

Two hundred and fifty new cases were seen in the course of nine months. These cases were predominantly in children and young adults from families in the lower-income classes, and the reason for their attendance was suspected malnutrition found by the school physician. It was to be expected, therefore, that nutritional deficiencies would be found in these persons.

Analysis of their diet on a sample day, usually that preceding the day of their attendance in the clinic, showed in fact that a great proportion of them had an intake of riboflavin of less than the recommended daily allowance of the National Research Council.[38] In this group, 72 children (29 percent) had a riboflavin intake of 80 percent or less. In spite of this, the incidence of corneal vascularity was very low.

Altogether 12 cases of corneal vascularity were seen. Only one of them had had a deficient riboflavin intake on the sample day, the others gave a satisfactory account of their diet, but it must be pointed out that no record could be obtained of their previous diet. What is more relevant is that six of them, who could be induced to attend the clinic regularly, were treated with riboflavin (15 mg. daily by mouth), and that all six responded to treatment. The vascularity became invisible within 2 to 4 weeks.

It is interesting to note, although no explanation can be found for it at present, that three of the cases of vascularization were obese young girls of 7, 12, and 17 years of age. They were put on a reducing diet of 1,200 calories a day which failed to influence the vascularity. When they were given 15 mg. riboflavin daily by mouth the vascularity disappeared within 3 to 4 weeks.

To return to the question: Does riboflavin deficiency always cause corneal vascularity? Of the 250 patients attending the clinic 29 percent had probably a riboflavin intake of 80 percent or less of the normal, and yet only about five percent showed corneal vascularity. This does not seem to provide an affirmative answer to the question.

An explanation may be found in a series of experimental observations. Williams and others[39] found no corneal vascularity in four subjects maintained for nine months on about 0.8 to 0.9 mg. of riboflavin per day. However, neither this amount nor about 1.1 mg. per day prevented a certain degree of depletion of tissue riboflavin as measured by load tests.

Keys and others[40] observed no corneal vascularity in their test subjects who for nearly six months were supplied with only about 0.9 mg. of riboflavin per day, and Davis and others[41] found that 0.6 to 0.7 mg. per day failed to cause corneal vascularization. About 1.3 mg. per day were required to prevent tissue depletion. Sebrell, Butler, and Wooley[42] found that 0.5 mg. per day was followed by corneal vascularization after 3 to 8 months.

It seems, therefore, that a low intake of riboflavin must continue for a prolonged period before anatomic signs of the deficiency and particularly corneal vascularity make their appearance. How low the tissue concentration of riboflavin has to fall in the cornea before corneal vascularization sets in has been shown experimentally by Bessey and Lowry.[43]

In rats on a riboflavin deficient diet the first signs of corneal vascularization ap-

peared only when the riboflavin concentration of the cornea fell to less than 50 percent of the normal. In rats on a completely riboflavin-free diet this stage was reached in three weeks, but in animals on a diet containing only slightly less than the optimum it needed a considerably longer time.

These studies and experiments may explain why our patients with an inadequate riboflavin intake failed to show corneal vascularity. Inadequate as it was compared with the recommended daily allowances, it was still sufficient to prevent a serious depletion of the cornea over the period of observation. The absence of corneal vascularity in patients on a diet moderately deficient in riboflavin is not a contradiction to the statement that riboflavin deficiency always causes corneal vascularization—if it lasts long enough to produce a low enough riboflavin concentration in the tissues.

Why is it, then, that patients with a low but not absolutely deficient riboflavin intake show vascularity of the cornea at all? In view of the foregoing it would require a very long period of time with a very low riboflavin intake, in fact an intake which is extremely unlikely to have existed for any very long period of time among the patients of our survey.

Observations on a group of seven patients (Table 1) not included in the Nutrition Clinic figures provide an answer to this question. These cases were selected in the Special Cornea Clinic of the Manhattan Eye, Ear, and Throat Hospital because of a pronounced degree of corneal vascularity. Some of them had undergone a corneal graft operation which was followed by vascularization of the graft, others had been attending the clinic prior to an intended corneal graft operation for corneal opacities acquired in the course of an earlier corneal disease.

The most interesting cases in this group are Cases 2, 4, and 5. These patients showed corneal vascularity after corneal graft operation while the second eye was normal. Their riboflavin intake was inadequate, but not grossly so, and the riboflavin level in the urine was low but not on a serious deficiency level. Each presented a heavily vascularized cornea which endangered the result of the operation. Such a relatively mild riboflavin deficiency would not be expected to cause corneal vascularization, and the unoperated eye failed to show it. Only the eye which had undergone surgical trauma displayed vascularity.

This vascularity responded most satisfactorily to riboflavin administration. Within 4 to 6 weeks all corneal vessels, even the deeper ones, became less engorged, the circulation became sluggish, "beading" made its appearance which indicates that blood corpuscles are captured in capillaries which close down, and the smaller vessels became

TABLE 1

OBSERVATIONS ON PATIENTS IN THE SPECIAL CORNEA CLINIC

No.	Daily Intake	Riboflavin Output	Operated on		Vascularity in		Result of Riboflavin Therapy
			R.E.	L.E.	R.E.	L.E.	
		(in gamma)					
1	61%	250	x	x	x	x	Excellent
2	39%	135		x		x	Excellent
3	70%	250	x	x	x	x	Good
4	39%	250		x		x	Excellent
5	54%	220	x		x		Good
6	90%	900	Mooren's ulcer both eyes with extensive vascularization				None
7	100%	440	Healed T.B. keratitis with vascularity after graft operation				None

to a large extent invisible. The general injection of the conjunctiva and the photophobia improved to the same degree. This response to riboflavin is highly significant.

Pirie[44] has pointed out that riboflavin fulfills a special function in the organism, and that its therapeutic use can only be expected to be effective when these specific functions are upset. The beneficial effect of riboflavin in corneal vascularity after corneal operations must therefore be due to a riboflavin deficiency which had not reached a degree sufficient to cause spontaneous vascularization; in fact, the unoperated eye failed to show it. It cannot be argued that any healing of tissue injury is accompanied by a growing-in of blood vessels into the traumatized area because this does not apply to the cornea. Vascularization after corneal transplantation is an abnormal and alarming sign which usually precedes an opacification of the graft.

Jolliffe[45] insists that biochemical changes and an impairment of function usually precede morphologic changes in deficiency conditions. Corneal vascularity is a relatively late result of these changes and the expression of a well-established deficiency. It represents the response of the organism to a degree of impairment of function which makes the continuation of normal metabolic processes impossible.

A deficiency disease may not be caused primarily by an inadequate diet but by interference with absorption or utilization of the essential nutrients, or by increased requirement, destruction, or excretion. Jolliffe has termed these states "conditioned" malnutrition.

In the case of corneal vascularization after surgical trauma to the cornea, the trauma can be regarded as the conditioning factor. The healing process after the operation causes increased activity of the corneal epithelium and stroma with a correspondingly higher oxygen requirement. In the presence of a nutritional deficiency of riboflavin, a point is reached sooner or later where the respiratory enzyme, of which riboflavin is a prosthetic group, is unable to keep up a sufficient oxygen supply.

An injured cornea thus requires more oxygen, consequently more respiratory enzyme, and therefore more riboflavin than a healthy one. A degree of riboflavin deficiency which remains subclinical under normal conditions will lead to corneal vascularization, which relieves the respiratory deficit, when pathologic conditions have caused the corneal metabolism to be on a higher level.

It has been shown by Lowry and Bessey[46] that a prolonged deprivation of riboflavin causes a definite handicap to the healing process of experimental corneal lesions.

It can be concluded that a relative riboflavin deficiency, which was too mild to cause either corneal vascularity in the healthy eye or other signs—glossitis, dyssebacia of the nasolabial fold, cheilosis—was the cause for the vascularization of the cornea in the eyes which had undergone an operation. The cases which had an adequate riboflavin intake and a normal riboflavin level in the urine were of a different etiology (Mooren's ulcer, tuberculous keratitis) and failed accordingly to respond to riboflavin medication.

The practical conclusions from these facts are obvious—every patient for corneal graft operation should be investigated as to his dietary habits and riboflavin should be administered pre- and postoperatively as a matter of routine. This routine has been followed with advantage by Franceschetti[47] and Rosso.[48]

The conditioning factor can assume different forms. While examining unselected patients in Palestine, I found a considerably higher prevalence of aribоflavinotic corneal vascularity among them than among the selected, malnourished patients of the Nutrition Clinic of New York City Health Department. I do not believe that this is due to a less satisfactory diet among the patients in Palestine; the very high incidence of seasonal Koch-Weeks conjunctivitis and trachoma in Palestine probably puts an extra strain on

the corneal metabolism and represents a conditioning or precipitating factor for the corneal vascularization.

The same applies to phlyctenular keratitis as shown by Landau and me; in this instance a subclinical riboflavin deficiency is conditioned by an allergic reaction and results in the so-called phlyctenular pannus which is nothing but the typical vascularization of ariboflavinosis. In a case report on a patient who had developed heavy vascularity of the cornea caused by a serious riboflavin deficiency conditioned by superficial corneal injuries I[49] arrived at the same conclusions. And finally, I observed a patient with maximal vascularization of the cornea in chronic riboflavin deficiency, conditioned by an acute sore throat with high fever which increased the riboflavin requirements of the organism.[50]

This, then, is the answer to the question why not every case of nutritional riboflavin deficiency displays signs of corneal vascularity. Unless the deficiency has reached considerable proportions, or *unless a conditioning factor comes into play*, corneal vascularity will fail to appear.

Summary

1. Corneal vascularity is a condition in which newly formed blood vessels enter the normally avascular corneal periphery; limbic congestion and circumcorneal injection may be early stages, but they are nonspecific and not pathognomonic for ariboflavinosis.

2. Corneal vascularity of riboflavin deficiency is of a type not observed in any other known clinical condition and is pathognomonic.

3. Riboflavin deficiency always causes corneal vascularity—if it lasts long enough to produce a low enough riboflavin concentration in the tissues.

4. The appearance of corneal vascularization may be precipitated by conditioning factors such as chemical or mechanical trauma to the cornea in the presence of a subliminal riboflavin deficiency.

3 Hopper Street.

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References

1. Bessey, O. A., and Wolbach, S. B.: J. Exper. Med., **69**:1, 1939.
2. Sydenstricker, W. P., et al.: J.A.M.A., **114**:2437, 1940.
3. Kruse, H. D., Sydenstricker, V. P., et al.: Pub. Health Rep., **55**:157, 1940. Sydenstricker, V. P.: Am. J. Pub. Health, **31**:344, 1941.
4. Leber: In Graefe-Saemisch's Handbuch, **2**:2, 1903.
5. Gregory, M. K.: Brit. M. J., **2**:134, 1943.
6. Ferguson, W. J. W.: Lancet, **1**:431, 1944.
7. Mann, I.: Am. J. Ophth., **28**:243, 1945.
8. Stern, H. J.: Acta med. orient., **6**:322, 1947.
9. Duke-Elder, W. S.: Textbook of Ophthalmology, St. Louis, Mosby, 1938, v. 2, p. 1724.
10. Johnson, L. V., and Eckhardt, R. E.: Arch. Ophth., **23**:899, 1940; **24**:1001, 1940.
11. Fish, W. M.: Brit. J. Ophth., **27**:107, 1943.
12. Wise, G.: Am. J. Ophth., **26**:591, 1943.
13. Stern, H. J., and Landau, J.: Am. J. Ophth., **31**:1619, 1948.
14. Landau, J., and Stern, H. J.: Am. J. Ophth., **31**:952, 1948.
15. Follis, R. H., Jr., Day, H. G., and McCollum, E. V.: J. Nutrition, **22**:223, 1941.
16. Orent-Keiles, E., and McCollum, E. V.: J. Biol. Chem., **133**:75, 1940.
17. Stannus, H. S.: Brit. M. J., **11**:103-104, 1944.
18. Goldsmith, G. A.: South. M. J., **36**:108, 1943.
19. Kodicek, J. H., and Yudkin, J.: Lancet, **2**:753, 1942.
20. Keath-Lyle, T., Macrae, T. F., and Gardiner, P. A.: Lancet, **1**:393, 1944.
21. Machella, T. E., and McDonald, O. R.: Am. J. M. Sc., **205**:214, 1943.
22. Pett, L. B.: Canad. M. A. J., **49**:293, 1943.

23. Tisdall, F. F., McCreary, J. F., and Pearce, H.: Canad. M. A. J., **49**:5, 1943.
24. Youmans, J. B., et al.: Tr. A. Am. Physicians, **57**:49, 1942.
25. Scarborough, H.: Brit. M. J., **2**:601, 1942.
26. Scott, J. G.: J. Royal Army M. Corps, **82**:133, 1944.
27. Wiehl, D. G., and Kruse, H. D.: Milbank Mem. Fund Quart. Bull., **19**:214, 1941.
28. Sandstead: Pub. Health Rep. **57**:1821, 1942.
29. Anderson, R. K., and Milam, D. F.: J. Nutrition, **30**:11, 1945.
30. Boehrer, J. J., et al.: Am. J. M. Sc., **205**:544, 1943.
31. McCreary, J. V., et al.: Canad. M. A. J., **51**:106, 1944.
32. Stannus, H. S.: Lancet, **1**:352, 1940.
33. ———: Brit. M. J., **1**:103, 1944.
34. Vanotti, A.: Schweiz. med. Wchnschr., **74**:309, 1944.
35. Pirie, A.: Brit. J. Ophth., **27**:291, 1943.
36. Pollak, H.: Brit. J. Ophth., **29**:288, 1945.
37. Borsook, H., Alpert, E., and Keighley, G. L.: Milbank Mem. Fund Quart. Bull., **21**:115, 1943.
38. Nat. Res. Council, Reprint and Circular Series, No. 129, 1948.
39. Williams, R. D., et al.: J. Nutrition, **25**:361, 1943.
40. Keys, A., et al.: Am. J. Physiol., **144**:5, 1945.
41. Davis, M. V., et al.: J. Nutrition, **32**:143, 1946.
42. Sebrell, W. H., et al.: Pub. Health Rep., **56**:510, 1941.
43. Bessey, O. A., and Lowry, O. H.: J. Biol. Chem., **155**:635, 1944.
44. See Reference 35.
45. Jolliffe, N.: J.A.M.A., **122**:299, 1943.
46. Lowry, O. H., and Bessey, O. A.: J. Nutrition, **30**:285, 1945.
47. Franceschetti, A., and Doret, M.: Bull. et mém. Soc. franç. d'Opht., **59**:83, 1946.
48. Rosso, S.: Vitaminologica. Milan, 1947, p. 1.
49. Stern, H. J.: Arch. Ophth., **42**:438, 1949.
50. ———: Ophthalmologica, **114**:103, 1947.

Ophthalmic Miniature

To George Whately

Passy, 23 May, 1785

. . . By Mr. Dolland's saying that my double spectacles can only serve particular eyes, I doubt he has not been rightly informed of their construction. I imagine it will be found pretty generally true, that the same convexity of glass, through which a man sees clearest and best at the distance proper for reading, is not the best for greater distances. I therefore had formerly two pairs of spectacles, which I shifted occasionally, as in travelling I sometimes read, and often wanted to regard the prospects. Finding this change troublesome, and not always sufficiently ready, I had the glasses cut and half of each kind associated in the same circle. By this means, as I wear my spectacles constantly, I have only to move my eyes up or down, as I want to see distinctly far or near, the proper glasses being always ready. This I find more particularly convenient since my being in France, the glasses that serve me best at table to see what I eat not being the best to see the faces of those on the other side of the table who speak to me; and when one's ears are not well accustomed to the sounds of a language, a sight of the movements in the features of him that speaks helps to explain; so that I understand French better by the help of my spectacles. . . .

B. Franklin.

NOTES, CASES, INSTRUMENTS

CORNEAL DERMOID*

REPORT OF A CASE

P. N. SINHA, M.B., AND S. MISHRA, M.B.
Patna, India

History. A Hindu boy, aged eight years, was admitted to the Prince of Wales Medical College Hospital on April 21, 1948, with the following complaints: (1) A tumor invading the cornea from the temporal half of the conjunctiva, leading to disturbance of vision in the left eye; (2) a tumor in the center of the right eye obscuring vision totally; (3) a deficiency of the upper lid of the right eye; (4) recurrent attacks of pain with redness and ulceration over the tumor of the right eye.

At his birth in 1940, the patient had a deficiency in the medial half of the right upper lid and forward bulging of the central part of the right eye. Vision was sufficient in the left eye but markedly diminished in the right eye.

In 1942, the bulging in the right eye became opaque and cream colored with a total loss of vision. At this time, a small, cream-colored bulging was noticed in the temporal half of the left eye. There was no redness in the eyes and no ulceration over the bulging in the right eye.

During the early months of 1948, the small tumor began a progressive invasion of the cornea of the left eye. Since total loss of vision was feared, medical aid was sought. Family history was noncontributory.

Examination of right eye. A quadrate-shaped coloboma (14 mm. wide and 8 mm. deep) of the medial half of the upper lid extended to the orbital margin in the extreme medial aspect. The lid margin was smooth and without lashes. The punctum lacrimalis and lashes were present in a three-mm. lobule medial to the coloboma.

A spheroconical tumor 10 mm. by 8 mm. involved the entire cornea except a narrow upper rim. The tumor was fixed, yellowish, dull, opaque, soft, and elastic with a few small hairs on the surface. It did not encroach anywhere beyond the limbus.

An oblong (13 mm. by 8 mm.) soft, elastic, yellow, opaque, movable tumor was opposite the lateral half of the palpebral aperture, a little away from the limbus and

Fig. 1. (Sinha and Mishra). Preoperative appearance of patient.

more in the upper and the outer zone. Its surface was dull and covered with a few small hairs more marked opposite the palpebral fissure.

Lacrimation was present; tension was normal; vision was reduced to perception of light and projection of rays.

Examination of left eye. A soft, elastic, dull, opaque, yellowish, oval (11 mm. by 7 mm.) tumor covered with a few minute hairs invaded the cornea from the temporal half of the bulbar conjunctiva. It had approached nearly opposite the pupillary area. The part over the conjunctiva was slightly movable, that over the cornea fixed.

Anterior chamber, iris, pupil, lens were all normal; tension was normal; distant vision was 6/24.

Physical examination. Accessory auricles were present on both sides. Examination of the ears, nose, and throat revealed en-

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larged septic tonsils and obstructive deafness of the left ear. Blood Wassermann was negative.

Provisional diagnosis was that the tumor masses were dermoids.

Comment. A dermoid is a solid tumor characterized clinically by a superficial skin-like covering with presence of hairs and pathologically by the presence of "mesoblastic tissue (fibrous and fatty usually) covered by ectoderm (skin) and invaded by its derivatives (hair follicles, sweat and sebaceous glands[1])." It has to be distinguished from: (1) *Dermoid cyst,* which is a cystic tumor formed by the invagination of the epithelium at the embryonic fissures, the cyst cavity being lined with ectoderm invaded by its derivatives. (2) *Congenital epithelial plaques* which contain layers of stratified epithelium without the skin derivatives like the hair follicles, sebaceous, and sweat glands. The corium element is also absent.

Fig. 2 (Sinha and Mishra). Photomicrograph of biopsy specimen from corneal dermoid.

A dermoid may be situated on the cornea, the conjunctiva, or the limbus, extending over both cornea and conjunctiva. It may be attached to cornea or conjunctiva alone or may be fixed to the sclera or uveal tract. A dermoid may even replace the lens.

"Apart from their occurrence in the rudimentary microphthalmic eyes or in staphylomatous pseudocornea, dermoids in the center of the cornea are rare."[2]

Mitvalsky,[3] out of 75 published cases found only five cases which were pure corneal dermoids. Two cases were reported by Stark[4] and by Gronholm.[5] Chan[6] reported a case of corneal dermoid in a guinea pig and Khan[7] in a pig. Wood[8] reported a case of corneal dermoid in a baby. Other case records of pure corneal dermoid are by Swanzy and Leber[9] (1871), Hanke[10] (1904), Stargardt[11] (1917), Mann[12] (1930), and Wilson[13] (1939). Although this list of reported cases is not complete, still, unlike conjunctival or limbal dermoids, not many cases of pure corneal dermoid are on record.

A dermoid is thought to be formed by an aberration in the mesoblast lying between the surface ectoderm and the optic cup. The resulting deformity varies with the time at which the aberration takes place. There are three grades of severity: (1) Small fibro-fatty tumor occurring astride the limbus, (2) whole of the cornea is replaced by fibro-fatty tissue which protrudes between the lids and is covered with skin and often hairs; (3) dermoid replaces all the tissues normally formed between the pigment epithelium of the iris and the surface ectoderm. In these cases there is no anterior chamber, no iris, and sometimes no lens. The case herein reported belongs to Grade 2.

Treatment. On April 26, 1948, the excision of the dermoid in the left eye was undertaken. The junction of the dermoid and the normal cornea was incised. The dermoid was dissected from the cornea and subconjunctival tissue and excised. The conjunctiva was mobilized and sutured over the wound. Mercurochrome and liquid paraffin drops were administered. The eye was bandaged. Recovery was uneventful in 10 days' time. When the patient left the hospital the distant vision in the left eye was 6/24.

On June 5, 1948, excision of the corneal dermoid in the right eye was undertaken. Incision was made along the junction of the growth and the healthy rim of the cornea. The growth was dissected away completely from the deeper layers of the cornea and then excised. The underlying remaining layers of the cornea were transparent.

(From the depth of dissection it was estimated that the tumor arose from the deeper layers of substantia propia. Enucleation of the eyeball was not consented to and every effort was made to preserve the normal cornea. Thus its inclusion in the excised mass was not possible. Histologic confirmation of the depth of growth was lacking.)

A round, central, regular, dark pupil and well-formed anterior chamber were noticed. The cornea was not cauterized. The lower lid was pulled over the coloboma and a temporary tarsorrhaphy was done.

The wound was bandaged without any drops. On the following day penicillin drops were started every two hours and were continued for a week. Mercurochrome (one percent) and liquid paraffin drops were subsequently used. The cornea became hazy and later turned opaque. Otherwise, the recovery was uneventful. Tarsorrhaphy stitches were removed after two weeks. Repair of the coloboma is under contemplation.

Biopsy report. Histologic examination of the paraffin section of the growth removed from the cornea of the right eye showed: Keratinization of the superficial layers of stratified epithelium. Typical skin layers with rete cones and pigmentation of basal layer. Underlying fibro-fatty layer showing heavy round-cell infiltration, preponderance of fibrous tissue, hair follicles, sweat glands, sebaceous glands, and blood vessels. Fatty tissue abounded in the deeper layers.

Histologic examination of the paraffin section of the corneoconjunctival dermoid of the left eye showed: Keratinization of the superficial layers of stratified epithelium. Typical skin layers with rete cones and pigment in basal layer. Underlying the epithelium was the fibro-fatty layer interspersed with hair follicles, sebaceous glands, and sweat glands.

Comments. Histologic examination of the microsections confirmed the tumors to be dermoids. The deeper layers of the cornea in the right eye were healthy and transparent and there was no adhesion between the iris and the cornea. Therefore, the possibility of this case being a case of congenital staphyloma with secondary dermoid formation like the case reported by Bernheimer[14] (1887) was eliminated.

The patient had occasional attacks of redness with ulcer formation on the corneal tumor in the right eye. This explained the subepithelial, heavy round-cell infiltration shown in its microsection. Exposure of the dermoid due to the coloboma accounted for the recurrent dermatitis, ulcerations, and conjunctivitis. Since the tumor of the left eye was not exposed, no such complaints occurred in that eye and no round-cell infiltration was found in its microsection.

Discussion

As to the causation of dermoids various theories have been put forward; not many of them are simple and none are explanatory of all cases of dermoids.

Ryba[15] (1853) was the first to use the term, dermoid, to designate this class of tumors. Many dermoids are situated opposite a coloboma of the lid. He explained that the formation of the growth is due to exposure.

Collins and Mayou[16] argue that, in cryptophthalmos, skin is formed in front of the eyeball due to exposure. Here is a condition that parallels dermoid formation. They argue that, even in the absence of colobomas, the eyeball may be exposed unduly at one or another stage of development and lead to dermoid formation.

In cases of metaplasia, though the nature of the epithelium changes, ectodermal derivatives like hair, sebaceous and sweat glands are lacking; nor is there any change in the

subepithelial layers. In cases of cornification of the conjunctiva or the cornea due to exposure or avitaminosis, the changes in the epithelium are similarly limited.

Contrasted with this, typical layers of skin with its derivatives are formed in cases of dermoid cyst, although the ectoderm is in no way exposed.

Simple exposure might explain the formation of congenital epithelial plaques but to attribute corionic changes to simple exposure is far-fetched. Furthermore, numerous cases of dermoids occur without colobomas and numerous cases of colobomas without dermoids.

Mann[17] is of opinion that dermoid formation might be earlier than the lid formation, its presence hindering the down growth of the lid fold and thus producing the notch.

Van Duyse[18] ascribed the dermoid formation to circumscribed adhesion between the amnion and the surface of the eyeball before the fourth month of intra-uterine life before the eye is covered by the lids. This theory of the implantation of amniotic bands is supported by Jansen[19] and von der Hoeve.[20] These bands are said to cause the formation of colobomas and accessory auricles. Support has been lent to this theory by observation that bundles of soft tissue sometimes connect the tumor to the different parts of the eyeball. Such bands are also attached to the face.

Fuchs[21] says that the amniotic band consists of simple connective tissue (mesoblastic). How could epiblastic tissue arise from it? In our case, although accessory auricles and dermoid were present on the left side, there was no associated coloboma of the lid.

Gallenga[22] proposes that dermoid may be formed when remnants of the plica semilunaris become implanted at a particular part of the cornea or the conjunctiva.

Fuchs[23] is of opinion that, in cases of oligohydramnios, the lids might be pressed by the amnion or the amniotic bands against the eyeball and cause implantation of a piece of the skin. This would take place before the last two months of intra-uterine life when the palpebral fissure is closed.

Castello[24] similarly proposed that the missing portion of the lid in a case of coloboma becomes implanted over the eyeball and causes dermoid formation.

How can we explain the dermoid formation in the left eye of our patient on the basis of the preceding theories?

Remak[25] proposed that it is the invagination of ectoderm which causes the formation of dermoid. If it were so, then the epithelial elements should have been situated quite deep and not superficially, as is the case with dermoid cyst.

All these theories explain the formation of dermoid attached to the superficial layers of the conjunctiva or the cornea. All of them ignore that dermoid may arise from deeper tissue like the sclera and uveal tract and may lead to the malformation or replacement of anterior chamber, iris, lens, choroid, vitreous, and even retina. This indicates that aberration occurs in the development of the mesoderm lying between the surface ectoderm and the lips of the optic cup. The surface ectoderm, instead of developing into cornea or conjunctiva, develops into skin in response to the abnormal developmental environment provided by the underlying mesodermal elements.

Dermoids do not occur in families and are not hereditary. Mechanical influences do not seem to be sufficient to alter the environment of the developing fetus and lead to this aberration. Physicochemical influences, including hormones, have been shown beyond doubt to produce congenital anomalies.

Hale[26] reports that vitamin-A deficiency is responsible for cases of anophthalmos and microphthalmos with congenital blindness. Interestingly enough his cases were associated with other abnormalities like accessory auricles, cleft palate, harelip, and so forth. It is possible that such a deficiency is responsible for the initiation of tissue aberration leading to dermoid formation.

SUMMARY

A case is reported with congenital coloboma of the right upper lid, congenital corneal and conjunctival dermoids in the right eye, congenital corneoconjunctival dermoid in the left eye, and accessory auricles on both sides.

The findings of the case, the operative treatment, and biopsy report are recorded. The various theories of the causation of dermoid are discussed with special reference to the case under report.

Prince of Wales Medical College.

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REFERENCES

1. Mann, I.: Developmental Abnormalities of the Eye. London, Cambridge Univ. Press, 1937, p. 379.
2. Duke-Elder, W. S.: Textbook of Ophthalmology. London, Kimpton, 1938, v. 2, p. 1407.
3. Mitvalsky: Arch. f. Augenh., **23**:109, 1881.
4. Stark: Am. J. Ophth., **2**:5, 1918.
5. Gronholm: Klin. Monatsbl. f. Augenh., **70**:771, 1923.
6. Chan, E.: Am. J. Ophth., **15**:525, 1932.
7. Khan, W. A.: Brit. J. Ophth., **10**:625, 1926.
8. Wood, D. J., and Scott, R. S.: Tr. Ophth. Soc. U. Kingdom, **45**:112 (Part I) 1925.
9. Swanzy and Leber: Dublin Quart. J. Med. Sc., 1875, p. 335.
10. Hanke: Arch. f. Ophth., **57**:28, 1902.
11. Stargardt: Ztschr. f. Augenh., **37**:25, 1917.
12. Mann, I.: Developmental Abnormalities of the Eye. London, Cambridge Univ. Press, 1937, p. 381.
13. Wilson: Giza Mem. Ophth. Lab., 1937, p. 8285.
14. Bernheimer: Arch. f. Augenh., **18**:171, 1888.
15. Ryba: Prager vieteljahrisch Jahrig, 1853, v. 3, p. 1.
16. Collins and Mayou: Pathology and Bacteriology of the Eye. Philadelphia, Blakiston, 1925, p. 142.
17. Mann, I.: Developmental Abnormalities of the Eye. London, Cambridge Univ. Press, 1937, p. 380.
18. von Duyse: See Chan, E.[6]
19. Jansen: See Mann, I.: Developmental Abnormalities of the Eye. London, Cambridge Univ. Press, 1937, p. 403.
20. v. der Hoeve: Tr. Ophth. Soc. U. Kingdom, **1**:237, 1930.
21. Fuchs: Textbook of Ophthalmology. London, Lippincott, ed. 5, p. 224.
22. Gallenga: See Chan, E.[6]
23. Fuchs: See Fuchs[21]
24. Castello, B.: Ann. d'Ottal., **53**:265, 1927.
25. Remak: See Chan, E.[6]
26. Hale: Am. J. Ophth., **18**:1087, 1935.

BINOCULAR CAMPIMETRY WITH COLORS*

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Central scotomas are difficult to outline accurately in many instances because of poor fixation. The patient is inclined to look at the fixation object with a paracentral area of the retina, shifting the point of observation to a part of more acute visual perception. In a former paper,[1] I described a colored chart which was especially useful for detecting small or relative scotomas. It was pointed out, however, that this chart would only demonstrate the central scotamas as such, and would not aid in outlining the shape of the scotoma, nor would it disclose the presence or absence of a paracentral scotoma.

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Lloyd[2] has described a binocular angioscotometer which is extremely valuable in detecting and outlining central scotomas and detecting paracentral scotomas. This instrument, however, is relatively expensive, and many ophthalmologists are not inclined to add this apparatus to their already extensively equipped offices. Special charts have been designed by Haitz[3] for detecting central scotomas on the stereoscope, but these charts are awkward for our purpose, for they require extremely close observation of the patient and do not allow a plotting of small angles.

In the method to be described, an eye with a possible central scotoma is tested on a tangent screen at 1 or 2 meters distance, while the patient observes the fixation point with the other (normal) eye. The affected eye observes a colored object; the fixating eye is covered with a glass of complementary color and will see the test object as colorless. Thus, the central scotoma in the uncovered eye will correspond to the area where the test object is seen as colorless, for no color will be seen in the area of the central scotoma. The test is performed with the complementary colors, red and green, and blue and yellow. Examination is restricted to observations with colors, but this is a finer test than the white test, and we can assume that at least a relative scotoma for white will correspond to the plotted color scotoma.

The test is only applicable when the patient has binocular vision, but an existing suppression will be easily recognized. The same reservation has to be made to test at the stereocampimeter. The hue of the colored glasses is chosen relatively light to avoid the elicitation of a phoria which would shift the scotoma correspondingly.

In looking through the literature, we found that Schloesser[4] had used this same arrangement of a glass with a complementary color to that of the object for binocular testing on the perimeter. Landoldt[5] commented favorably on this procedure. Apparently, the method was forgotten, however, because no reference could be found to it in Peter's or Traquair's books on perimetry. The simplicity and accuracy of this method for plotting a central scotoma prompted its recommendation for application to the tangent screen.

Summary

The central field of an eye is examined with a colored object. The other eye is covered by a glass of the complementary color. Thus, the normal eye which is covered by a colored glass, acts as the fixing eye and sees the test object as colorless, while the uncovered eye observes the color in the test object outside of the area of the central scotoma. In this way the central color field is tested and a scotoma is easily plotted.

350 Post Street (8).

A set of objects (1, 2, 3 and 5 mm.) and 4 glasses which fit into a trial frame in the complementary colors red and green, and blue and yellow, are available at A. H. Parsons Laboratory, 518 Powell Street, San Francisco.

References

1. Engel, S.: Colored charts as a supplementary test for macular vision. Arch. Ophth., 24:910, 1940.
2. Lloyd R. I.: The stereoscopic campimeter. New York State J. Med., 112:944, 1920.
3. Haitz, E.: Binoculäre Untersuchung d. Gesichtsfeldzentrums vermittels d. Stereoskops. Klin. Monatsbl. f. Augenh., 42:321, 1904.
4. Schloesser, C.: Sammlung Zwangl. Abhandl. a.d. Gebiete d. augenh., III, Heft 8, 1901.
5. Landoldt, E.: Die Untersuchungsmethoden. Graefe-Saemisch IV, 1. Abtlg. 1904, p. 537.

REVALUATION OF THE SNARE TECHNIQUE FOR ENUCLEATION

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The use of the tonsil snare in enucleation is nothing new, but has certain practical points in its favor. A review of the procedure is timely and well worth careful consideration.

The removal of an eye with the snare has one specific advantage over removal with scissors and this is that Tenon's capsule is left intact and not cut, as is so frequently done when severing the optic nerve with scissors. Frequently, when using the scissors, rents are cut in the posterior part of Tenon's capsule. This is not desirable when an implant is going to be used, particularly the Stone-Jardon type, for the freer the capsule is from trauma or rents, the better will be the movements of the implant. The more freely the implant moves, the better the cosmetic effect.

A second factor recommending the use of the snare is that, when properly applied there is practically no bleeding. When the posterior ocular vessels are severed together with the optic nerve, it permits the operator to proceed immediately with the placing of an implant into Tenon's capsule. Thus, a period of from 5 to 15 minutes is eliminated in bringing bleeding under control. This is important when one has a patient under general anesthesia, particularly when instilling an implant of the Stone-Jardon type which takes a much longer time compared with the procedure for implantation of a plain plastic ball. If the snare is properly applied and the optic nerve and vessels are crushed and cut, in the majority of cases no bleeding will occur when the eye is enucleated.

TECHNIQUE RECOMMENDED

The technique found most suitable is: The conjunctiva is opened around the limbus as in any routine enucleation. Then the four rectus muscles are picked up with the squint hook and white-silk, 4-0 sutures are inserted into each rectus tendon; each muscle is severed at its tendonous insertion after the sutures are in place.

The next step is to pick up the inferior oblique and superior oblique muscles with the squint hook and tenotomize them. It is important to tenotomize the obliques with scissors because this makes the application of the snare around the eye easier, with less pressure exerted on the globe and its contents. The obliques are rather hard to cut with a snare and often require the application of so much force on the wire loop that it will break or pull out of the snare shaft; also, when heavy pressure is exerted, the muscles may cut suddenly with the vessels and optic nerve included, causing one to lose the desired crushing and sealing effect. If the obliques are properly cut there will be very little extraocular pressure exerted on the intraocular contents of the globe when the snare is closed. This makes soft, lacerated eyes and eyes with weak scleral tunics easily enucleated, if traction is put on the eye anteriorly with a fixation suture in the stump of the internal rectus tendon proptosing the eye forward while the snare is slowly closed.

After the obliques are cut, a fixation suture (4-0) is placed into the stump of the internal rectus tendon, then the wire loop is drawn up to the size that will just snugly pass around the globe. The shank of the snare is gradually pushed backward into the orbital cavity from the temporal side in close contact with the globe as the operator closes the snare slowly while the assistant makes sure the rectus muscles and Tenon's capsule are outside the wire loop. Traction anteriorly by pulling forward with the fixation suture, producing a mild proptosis of the globe, prevents the snare from including a portion of the sclera around the optic nerve in soft or collapsed eyes.

The most important step is the final closure of the snare. It should be closed to almost the point of severance of the optic nerve and held for about 30 seconds. This has a crush-

ing rather than cutting effect on the vessels that completely controls all bleeding from the posterior ciliary arteries, central retinal artery, and vein. This step is easily mastered because the operator quickly develops a sense of feel denoting the point when the optic nerve is well crushed.

Another point in favor of the snare technique is that it is not necessary to use a tight pressure bandage to prevent postoperative hemorrhage into Tenon's capsule with possible expulsion of implant. The patient may be out of bed after he has recovered from the anesthesia.

SUMMARY

The snare technique in enucleation has the following points of advantage over scissors:

1. Less traumatism to posterior one third of Tenon's capsule and no lacerations occur.
2. No bleeding when eye is enucleated saving 5 to 15 minutes on operating time.
3. Control of postoperative hemorrhage, making negligible the possibility of extrusion of the implant.
4. Tight uncomfortable pressure dressing not necessary.
5. Patient may be out of bed as soon as he has recovered from anesthesia. Any operator who uses this technique a few times will be well pleased with it and will use it to replace the scissors in most of his enucleation procedures.

1720 Exchange Building (3).

PTOSIS WITH ELEPHANTIASIS AND ECTROPION*

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Beard[1] tells us that "advancement, or shortening the levator, by making a fold therein, was first suggested by Bowman . . . and first practised by Everbusch of Munich (in 1883)." He also credits Snellen of Utrecht with the first resection of the levator tendon. Since then there have been innumerable modifications of the original techniques, including the now classical Everbusch procedure. Of these modifications probably the most popular is that of Blaskovics[2] who, in 1923, first suggested tarso-levator resection by the conjunctival route. Since then, many variations of this latter procedure have in turn found their way into the literature.

The rare case of ptosis reported here in which a Blaskovics approach was used is presented because of the bizarre history, the unusual combination of deformities it presented, and the unexpectedly fortunate results obtained.

CASE REPORT

History. E. C., a 12-year-old Negro boy, was first seen in March, 1948. At the age of 18 months he was struck in the right eye with a baseball. A few weeks later, the right upper lid began to swell and the eye to close. This condition progressed until the eye was completely closed and has remained so since.

On March 31, 1939, he was admitted to the Manhattan Eye, Ear, and Throat Hospital where a biopsy of the lid swelling was made. The pathologic diagnosis was plexiform neuroma. The vision at that time was 20/40 in the right eye and 20/30 in the left eye. He was discharged April 4, 1939.

On January 22, 1947, he was admitted to Metropolitan Hospital for a "lump on his right eyelid" after having been treated at Memorial Hospital for fibromatosis involving the right orbit and temple (date not specified).

Because of right-sided convulsive seizures, right hemiparesis, and possible left cortical atrophy (X ray) a craniotomy was done through a left temporoparietal flap. A subarachnoid cyst was found and drained. A local pachymeningitis was also found. The patient was discharged on April 23, 1947. He was readmitted to Metropolitan Hospital on July 15, 1947, with a diagnosis of ptosis

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and elephantiasis of the right upper lid. At operation on July 29, 1947, "scar tissue was excised from the right upper lid." The pathologic diagnosis was nonspecific fibrous tissue. He was discharged on August 1, 1947.

Physical examination. When seen in March, 1948, the boy appeared underdeveloped. He was mentally retarded and had been a behavior problem in school. The right arm was atrophic and held in flexion across the chest. There was a soft, irregular, nontender mass anterior to the right ear.

Eye examination. The right upper lid was twice the normal size and covered the eye completely (fig. 1). The lid was twice the normal thickness and the palpebral fissure measured 45 mm. in length. There was an ectropion with thickening and excoriation of the exposed conjunctiva as is usually seen in cases of long standing. There was a horizontal scar, 5.0 cm. in length, running along the lower border of the right eyebrow. Despite all this there was slight movement of the lid on looking upward, though not enough to uncover any part of the cornea.

The best obtainable vision was: R.E., 20/100, with the lid held up; L.E., 20/25. There was limitation of rotation of the right

Fig. 1 (Fox). Appearance of patient before operation.

eye in all directions. The fundus was negative.

X-ray studies of the orbits showed normal optic foramina but there were "sclerotic changes adjacent to the right orbit externally." X-ray studies of the skull showed "a sella larger than normal with the posterior portion widened." No destructive pathologic process was noted.

Operative procedure. On March 4, 1948, a modified Blaskovics operation was performed under general anesthesia. On eversion of the lid the conjunctiva was found to be so thickened, discolored, redundant, and fibrotic that it was impossible to identify the upper edge of the tarsus clearly. A horizontal incision, 10 mm. from the lid edge, was made in the thickened conjunctiva and tarsus along the whole length of the lid with considerable difficulty and undermined upward for 15 mm. This tissue was so thick that it was everted and portions of it shaved off to thin it out. Much bleeding was encountered.

Fig. 2 (Fox). Appearance after first repair. Note good lid fold.

In place of the normally thin levator muscle a thick, fibrotic tissue was discovered which did not look as if it had any contractile elements at all. However, this was dissected up from the subjacent thickened orbicularis (more by guess than by anatomic appearance) as far back as it was possible to go, and a strip about 15 mm. in width was resected. Three double-armed, 4-0 plain catgut sutures were passed through the upper edge of the presumed levator which was then pulled down and sutured between the lower edge of cut tarso-conjunctiva and the skin-muscle layer. The conjunctiva was revised, a good deal of the redundancy resected and the cut edges sutured together with 4-0 black silk interrupted sutures.

Because of the difficulty encountered in

identifying tissues and because of the extensive dissection, the prognosis for success was not particularly good. It was gratifying, therefore, to note two weeks after operation that there was elevation of the right upper lid almost equal to that of the left upper lid. Not only that, but there was a good lid fold (fig. 2). However, there was still a protrusion of redundant, thickened conjunctiva although the ectropion had disappeared.

Six weeks later the excess conjunctiva was

Fig. 3 (Fox). Appearance after excision of redundant conjunctiva. Canthoplasty required.

resected with the result seen in Figure 3. The patient was now able to open and close his eyes normally. The palpebral fissure was still too long and the boy was told to return in four weeks for a final canthoplasty. He did not return. Five years from now he will probably drift into another hospital and the final repair will be made.

Comment

The obvious comment here, of course, is that no case however seemingly hopeless is necessarily so. Certainly the result here exceeded all reasonable expectations.

Another unusually interesting feature—at least to me—is the latent power residual in a levator which had been inactive for 10 years and had undergone tremendous fibrosis in addition. One can only postulate sufficient concomitant hypertropy of levator muscle fibers along with hypertrophy of the rest of the lid to retain a modicum of elevating function when given the chance.

It is also worth mentioning, I think, that however abnormal the conditions encountered, it is always wise to stick to basic techniques which have been found trustworthy. It is true that the techniques may have to be simplified. In this case the bare essentials of the Blaskovics procedure were employed. No attempt was made to use any of the surgical elaborations abounding in the literature—levator resection at its simplest was done. And Fortune smiled.

11 East 90th Street (28).

References

1. Beard, C. H.: Ophthalmic Surgery. Philadelphia, Blakiston, 1914, p. 238.
2. De Blaskovics, L.: A new operation for ptosis with shortening of the levator and tarsus. Arch. Ophth., **52**:563-573, 1923.

A NEW METHOD FOR EXPOSURE OF THE GLOBE IN CATARACT SURGERY

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It is a well-known fact, and one which may be easily demonstrated by even casual observation at the operating table, that the ordinary speculum used in cataract surgery frequently presses on the globe and causes an increase in intraocular pressure. Sometimes undesirable effects, such as the loss of vitreous, can be traced directly to this increased pressure.

A speculum is essentially rigid in its makeup and cumbersome to adjust, particularly during the course of an operation after the eye has been opened. At the end of operation even the removal of a speculum is not entirely free from danger, since the spring mechanism is often quite strong, and the manipulation of one blade moves the other. One

of us has seen an eye very badly damaged by the careless removal at the end of operation of a towel, which caught on the end of the speculum and levered it into the eye.

In view of these facts, we began to use lid sutures in intraocular operations. These too are not satisfactory.

The insertion of every suture means damaging of tissue, with possible subcutaneous ecchymosis, potential infection, and perhaps postoperative discomfort. The exposure is often accompanied by tenting, and occasionally the upper lid becomes everted, with undesirable pressure on the globe.

If only one suture in the midline is used, the exposure is sometimes inadequate and, if multiple sutures are used, the many threads constitute a nuisance. Once lid sutures are inserted they cannot be changed without being removed and reintroduced into the tissue.

The procedure described here was then developed. A Katzin aluminum suture mask is used. This is bent to conform to the patient's face and to fit securely. Anchoring of the mask is easily done by the application of mosquito forceps to the towel or drape sheet, one on each side, just inside the inner rim. Three holes drilled in each end of the mask (fig. 1) permit a towel to be clipped on either end, giving a very satisfactory stability to the position of the mask.

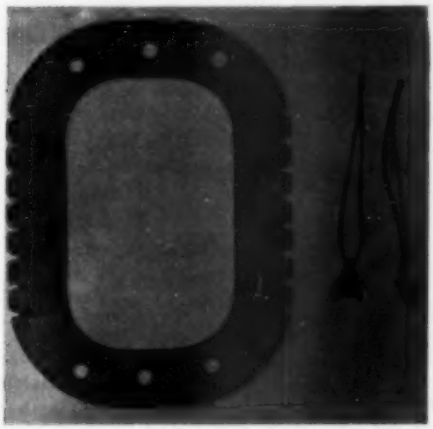

Fig. 1 (Muir and Kafka). The Katzin aluminum suture mask with three holes drilled in each end. Blades of the Guyton-Parke speculum with black-silk suture threaded through the hole at the end of each blade.

Two of the blades of the Guyton-Parke speculum were also modified. Since we do not tie the eye to anything, the projecting knobs were removed, and the smooth shiny surface was burred to prevent the reflection of the operating lights. A thread, passed through the hole in the end of each blade, is tied as shown in Figure 1. Any material is suitable for this; we use a medium-sized black-silk suture thread.

Fig. 2 (Muir and Kafka). A patient ready for operation with mask and blades in position.

After the usual preparation and draping, the mask is placed over the patient's face and one of the blades is inserted onto each lid. Mosquito forceps hold the thread from the upper blade over the top part of the mask and that from the lower blade over the lower part of the mask (fig. 2). The notches in the edge of the mask make it possible to use any direction of pull desired. We routinely use a suture through the superior rectus muscle,

and the ends of this are brought up over the top portion of the mask where they can be held, in any desirable direction with any desired amount of pull, under one of the notches in the edge of the mask.

The mask can be adjusted so that the blades not only do not touch the eyeball but also elevate the lids from the globe so that even their pressure is removed. Either one of the two blades can be moved independently and any desired traction, elevation, or sideway movement can be put on each.

After the palpebral aperture is obtained, this as a whole can be moved up or down by merely sliding the mask up or down. The lower blade can be removed in a matter of seconds without disturbing any of the other arrangements. The operative field is free from bars, screws, projections, or any other hindrances. There is no danger of any sudden change in tension due to a spring or set screw slipping.

If, during the course of surgery, it is necessary to move either blade to the right or left or to the midline, this can be done in a matter of seconds by merely shifting the thread from one notch to another. The blades themselves are small and thin, nonmagnetic and rustproof, and removal of the knobs prevents their getting in the way during surgery.

The time consumed in putting on the mask, anchoring it, putting in the blades, and getting them properly adjusted takes approximately one minute. Both hands of the operator and of the assistant are free. Any width palpebral opening may be easily attained. Although the palpebral opening will remain fixed, it can be quickly and easily modified. No pressure from the lids or blades is exerted on the globe, which is most desirable.

We have used this method for exposure of the globe in over 100 intraocular operations and are sure that (combined with close attention to premedication, anesthesia, and akinesia), operative complications have decreased, that technically the surgery is better and that the postoperative results have improved. It is the most versatile and desirable method with which we are familiar. We believe that, in most instances, the speculum not only has no place in intraocular surgery but should be discarded.

3705 East Colfax Avenue (6).
1820 Gilpin Street.

Ophthalmic Miniature

From the clear exposition of the best, unquestionably genuine, writings of Galen (born 131 A.D.), it is clear that the Greeks of old knew and practiced a cataract operation which was a displacement or depression of the lens, and also that a few physicians had risked the removal of the lens after incision of the eyeball. It is not mentioned who risked this, how he did it, or in what circumstances.

Hirschberg, *Graefe-Saemisch, Handbuch.*

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

SECTION ON OPHTHALMOLOGY

April 21, 1949

DR. PERCE DELONG, *chairman*

METASTATIC CARCINOMA OF THE EYE*

DR. JAMES N. GREEAR, Washington, D.C. (by invitation), presented a paper on this subject, a brief abstract of which follows:

Recent studies of groups of patients under treatment for carcinoma indicate that metastasis to the eye is more frequent than previously supposed and, further, that metastatic lesions in the eye are relatively more frequent from primary carcinoma of the lung than of the breast. The eyes of patients with primary carcinoma of the lung or breast should always be carefully examined for metastatic lesions.

Discussion. Dr. Wilfred E. Fry: I think that Dr. Greear has covered the subject of metastatic carcinoma of the eye very thoroughly. About all that I can do is to emphasize some of the interesting points that he has discussed.

I think he is correct in his view concerning the frequency of metastatic carcinoma. Many of these cases are not examined, because the patient is so ill that the generalized symptoms and prognosis so overshadow any ocular complaint that it is not examined in detail; in addition, relatively few of these patients go on to secondary glaucoma when the services of an ophthalmologist become urgent.

Another feature I think is interesting is the relatively great frequency of metastatic carcinoma of the eye when the primary tumor is in the lung. This is much higher than most of us had thought. In most cases that I recall the mammary gland has been the one which was the seat of primary tumor.

Another feature that was pointed out is that almost any structure of the interior of the eye may be involved in a metastatic lesion. Undoubtedly the structure most frequently involved is the choroid. Just because other structures are involved, we do not necessarily immediately have to jump to the conclusion that it cannot be a metastatic lesion.

Still another feature that I thought important was the fact that occasionally a tumor may occur in the eye and appear to be the primary tumor, whereas, in reality, it is secondary to a tumor elsewhere. If Dr. Greear would care to comment on it, I wonder if he could give us some more detail in regard to the cytology of some of these tumors in the eye. I think he mentioned one tumor of the lung in which the initial opinion was that the eye involvement was primary; whereas, a tumor in the lung was the primary lesion. It might be worthwhile to mention briefly the three ways in which, as I recall it, most of these tumors have exhibited themselves clinically. They are illustrated by three cases that have been under my observation at various times in the past.

These three manifestations are in brief: (1) Involvement in or near the macular region, (2) extensive retinal detachment, and (3) secondary glaucoma. As an illustration of the first case, there was a patient who had been under my care for some time, and whom I had refracted several times. The patient was a woman about 35 years of age. Her initial symptom was disturbance of vision, and the only ophthalmoscopic sign was some haziness in the macular region. In the course of time, this developed to the more or less typical appearance of a metastatic intraocular growth. The history aided in the diagnosis. There had been extensive surgical

* The paper, "Metastatic carcinoma of the eye," presented by Dr. Greear at this meeting, is published in full on page 1015 of this issue.

procedure for the removal of one breast for carcinoma but, at the time at which the ocular symptoms developed, a survey of her chest and other structures was entirely negative. She died about eight months following the first appearance of her ocular symptoms.

The second type of involvement is illustrated by another patient, a woman about 40 years of age, who had also had radical breast surgery three years previously. The cause for my seeing her was rather rapid loss of vision in one eye. At the time I saw her, there was extensive retinal detachment.

The third type, of secondary glaucoma, was illustrated by another patient that I had had under observation, in whom the secondary glaucoma followed rather rapidly on the initial appearance of choroidal lesions. The diagnosis was not difficult since X-ray studies of the spine revealed metastatic lesions. The eye had to be removed because of secondary glaucoma, and the patient died within a year.

I think we are indebted to Dr. Greear for this very excellent coverage.

Dr. John S. McGavic: Dr. Greear has, in his usual fashion, presented a very enjoyable as well as scientific paper. There are, I think, two reasons for the fact that available statistics do not reflect a higher incidence of metastatic lesions in the eye.

The first of these is that few ophthalmologists see more than 1 or 2 or 3 cases, and they are not likely to report them singly. The second is that the tumor specialists are not easily stimulated by unusual sites of metastatic tumor, nor do they look upon the ophthalmologist as cutting much of a figure in cancer work. They, therefore, do not invite us in when metastasis might best be seen. On the other hand, it has been pointed out that metastatic lesions sometimes appear before the primary tumor is suspected. Such a case has recently been sent to us by Dr. McDonald who removed the eye postmortem. The patient, aged 65 years, had a detachment of the retina in the upper portion. It involved the upper portion of the optic nerve, and we are told that the nerve appeared as though it were split. No operation was done, but a careful search for a primary lesion was made, because a metastatic lesion was suspected, and no primary tumor was found. The patient died shortly, and had bronchogenic carcinoma. This specimen was interesting, because of the fact that about 90 percent of the neoplastic tissue in the choroid was necrotic.

It has been my privilege to examine about eight patients with metastatic carcinoma, most of them at Memorial Hospital in New York. One of these had metastasis to the optic nerve which responded very promptly to radiation therapy with clearing of the field defects. The other two had metastases to the choroid with separation of the retina. These also responded to radiation therapy during the short survival of the patient.

Apparently the necrosis of the tumor caused by the radiation is responsible for the production of chorioretinal adhesions which can be seen developing during the period of treatment. Because the life expectancy of the patient is short, and the latent period for development of radiation cataract is long, this is an ideal situation in which to use radiation, and it can be extremely helpful in preserving or restoring vision in people whose lives are going to be not-too-happy from then on. The preservation of vision is especially appreciated by those who are otherwise incapacitated.

The manner of growth of metastases has been so well covered there is not much to say about it. Even though the lungs may be skipped, it is rather striking how many people whose tumors are not primary in the lungs do have pulmonary involvement either clinically or at postmortem, when they have ocular metastasis.

Both clinically and on section the separation of the retina in these cases seems to be far more extensive than it is with primary tumors of the same size such as malignant melanoma in which case the retina is commonly adherent to the tumor.

There are several situations in which one would suspect a metastatic lesion without other evidence: (1) If the detachment is bilateral, it would not be a melanoma. (2) If the detachment is very diffuse, and if there is any reduction in the transillumination, this area would be much smaller than the area of detachment. As you all know, transillumination in carcinoma is much less interfered with than in more solid tumors such as melanomas.

The third point I think is of even more practical significance—if there is a shift of the subretinal fluid when the patient is examined upright as opposed to the examination when the patient is lying flat, the probability of a metastatic lesion is greater. I know of two instances in which this was an impressive feature.

Some years ago we had about 45 sections collected from here and there showing tumors in the eye which were metastatic; 41 of these involved the choroid; one involved the optic nerve and choroid; two involved the choroid, iris, and ciliary body; and two involved the iris and ciliary body alone.

Of those that involved the iris there were eight, and only two involved the iris alone, while the remainder involved either the ciliary body or choroid, or both, together with the iris.

Why there is less involvement of the ciliary body than there is of choroid or iris alone has not been explained. In those that involve the iris, there is only one feature that seems distinctive, and that was illustrated by Dr. Greear, that the portion of the tumor extending to the posterior surface of the cornea is much more extensive than is usual in malignant melanomas or leiomyomas.

It is not unusual for people to have more than one malignant tumor. Therefore, it is not possible in all cases to decide which gave rise to the metastatic lesion while the patient is alive. For example, one patient had a radical mastectomy for carcinoma, and about 3 or 4 years later developed a tumor in the iris. The eye was removed, and supposedly there was a metastatic carcinoma, but it turned out to be a lymphoma. The patient was alive and well five years later showing no evidence of either carcinoma or lymphoma.

Two years is generally given as the longest time in which patients have survived, but von Sallmann has reported one who was alive three and a half years after enucleation. Such unusual instances lead us to the conclusion that one should treat these metastatic tumors actively. I do not believe I would take such a dim view of their prognosis although the patients are almost sure to die.

Since 20 percent to 33 percent of the tumors are bilateral, it would be, I think, a mistake to enucleate even one eye except for blindness or relief of pain. Furthermore, I believe that the primary lesions should be treated actively even if it requires major surgical treatment on the basis that we are not always so sure that the metastatic lesion is carcinomatous, and that it comes from the suspected source.

Yesterday, Dr. McDonald sent an interesting specimen to the laboratory. The patient was a 36-year-old woman who had had a mastectomy two years previously. There was no clinical evidence of metastasis elsewhere, but she had a detachment of the retina which appeared serous. Metastatic carcinoma was suspected by Dr. McDonald. There was no hole in the retina. Although the detachment appeared serous, no fluid was released at operation. A second operation was done, at the request of the patient, as the first was not successful. The second time no fluid was obtained so Dr. McDonald sent a trephine button of sclera and some attached tissue to the laboratory with the request that we look for carcinomatous cells, and such cells were present. This is rather an unusual situation.

Dr. Perce DeLong: In 1932, I had the pleasure of reporting a case of carcinoma of the choroid at this section. At that time I felt they were a rare pathologic entity, but several of my confreres in Philadelphia

stated to me that if I would come to certain hospitals, they would show me several cases. I proceeded to three institutions, and there I found advanced cases of carcinoma, usually bedridden, and to my amazement I found seven solid detachments of the choroid, which were in all probability metastatic manifestations.

The ophthalmologist does not, as a rule see these cases, because they are not ambulatory. I was informed that in many instances in the last stage of carcinoma, they have definite eye symptoms with reduction of vision and pain.

Dr. James N. Greear (closing): Dr. Fry stated that one of the interesting features about metastatic carcinoma involving the eye was the degree of pain which these patients apparently encountered even in the absence of glaucoma. This may occur when there is no rise in tension and the eye is relatively free from inflammatory disturbance.

It was interesting that five of the 44 cases studied at the Army Institute of Pathology complained of dimness of vision as the first symptom of the carcinoma. In some of these patients the eye was removed, because it was thought to contain a malignant melanoma.

In answer to Dr. DeLong's question, Dr. Greear said that he did not believe he had seen any cases of metastatic carcinoma of the eye arising from a primary carcinoma of the uterus. He emphasized the importance of radiation therapy when both eyes were involved, particularly when there was a life expectancy of a period of months.

He pointed out that, since detachment of the retina may occur early in metastatic carcinoma of the choroid, a bilateral detachment of the retina should make one suspicious of metastatic carcinoma.

A very considered judgment should be employed in advising surgery, particularly major procedures, when one can be relatively assured of general metastasis.

M. Luther Kauffman,
Clerk.

COLORADO OPHTHALMOLOGICAL SOCIETY

May 21, 1949

Dr. Fritz Nelson, *presiding*

Dislocation of lens

Dr. Guy L. Hopkins presented a case of bilateral outward dislocation of the lens, with fundi appearing normal. The vision in the right eye was 10/200, correctible to 20/200; left eye, 20/200, correctible to 20/80. One brother, the mother, and the maternal grandfather were also reported to have the condition unilaterally.

Discussion. Dr. Fritz Nelson suggested that better vision might be obtained by refraction of the aphakic portion of the pupil. The occurrence of the condition in Marfan's syndrome was pointed out.

Unilateral myopia

Dr. Hopkins also presented a case of unilateral myopia (−25.0D. with ophthalmoscope) with light perception only in that eye, the other eye being normal. In the discussion the uselessness of refraction was pointed out and the frequency of retinal detachment following removal of the lens was remarked upon.

Elevation of retina

Dr. W. T. Brinton presented a case of elevation of the retina in two places, laterally and inferiorly in the same eye. The patient had presented herself with the complaint of frontal pain and pain in the right side of her head. She also had had a subconjunctival hemorrhage in that eye.

Discussion. Dr. R. W. Danielson pointed out the contrast between the normal contour of the vessels over the upper area and the irregular contour and pallor of the vessels over the lower elevation, indicating the solid and serous elevations respectively. Since no hole could be found, and the upper elevation did not transilluminate, a differentiation was be-

ing sought between possible melanoma, subretinal hemorrhage, and Coats's disease.

Dr. G. H. Stine referred to Spaeth's work suggesting aspiration in suspected subretinal hemorrhage but felt that the eye should be removed if the general physical examination was negative, including a search for a hemorrhagic diathesis.

Further comment pointed out that the original pain might be due to a melanoma arising in the sheath of Schwann of the long posterior ciliary nerve and that corneal anesthesia might be present in the segment of the cornea served by that nerve.

Traumatic cataract

Dr. Harvey S. Rusk presented a man in whom he had removed a traumatic cataract which had been present for 71 years (since the age of eight years) and had obtained good vision. The fact that the eye had completed development at the age of eight years and that amblyopia ex anopsia had not developed was emphasized.

Retrolental fibroplasia

Dr. R. C. Richardson presented a six-month-old child with an opacity behind one lens since birth and a 21-month-old child with opacities behind both lenses.

Discussion. Dr. R. W. Danielson discussed some of the recent literature on retrolental fibroplasia, mentioning its occurrence unilaterally at birth in full-term infants and its development after birth bilaterally in premature infants. The possibility of the unilateral opacity being a retinoblastoma was unlikely as the eye was not microphthalmic and glaucoma had not developed. X-ray studies should also show calcifications in such a tumor.

Complications of eye injury

Dr. George H. Stine presented a 12-year-old boy who had been struck in the right eye in August, 1948, and had apparently recovered normal vision by November, 1948. On February 5, 1949, vision in each eye was 0.3. The right pupil was slightly larger than the left and reacted sluggishly. There was a faint aqueous flare with some breakdown of the anterior vitreous.

A solitary chorioretinitic mass about one prism diopter in diameter was situated between the disc and the macula. A small retinal hemorrhage was up and temporal from it. Fine glistening retinal striations extended throughout the macula. Subretinal hemorrhage was present around the nasal edge of the mass. A narrow curvilinear choroidal rupture extended from the lower portion of the mass nasalward below the disc. The remainder of the fundus was normal.

A thorough physical examination was negative for tuberculosis, undulant fever, foci of infection, and so forth. Slow absorption of the mass had been noted up to May 3, 1949, and vision was 20/200 plus. However, the mass was almost entirely absorbed by May 21, 1949. Boeck's sarcoid was suspected but could not be proved.

Melano-epithelioma of iris

Dr. R. W. Danielson presented the case of H. B., a 54-year-old woman, who was first seen on September 10, 1948. For four years she had noticed a black spot at the lower pupillary edge of the iris of the left eye. This had given no trouble and was not growing. On examination he found a definite thick pigmented mass involving the pupillary border which he considered to be a melanoma. On October 1, 1948, Dr. William E. Benedict removed the tumor by iridectomy and the pathologic report was melano-epithelioma of the iris.

The patient returned for observation on November 18 and December 16, 1948, and on January 24 and March 7, 1949, and on all these occasions there was no evidence of recurrence. However, on May 9, 1949, there was a small, dark, elevated mass in the angle of the anterior chamber nasally. The corrected and uncorrected vision was 20/30. The intraocular pressure (Gradle-Schiøtz) was 40 mm. Hg and was not lowered by miotics. Enucleation was recommended but

the patient refused because of the good vision and the lack of pain.

Thomas M. Van Bergen,
Recorder.

OPHTHALMOLOGICAL SOCIETY OF MADRID

March 18 and April 29, 1949

DR. MARIN AMAT, *president*

COLOBOMA OF THE OPTIC NERVE

DR. JOSE LUIS DEL RIO CABANAS presented a case of coloboma of the optic nerve of the right eye with a colobomatous excavation of the papilla of the left eye and an associated microphthalmia of both eyes. The patient, a woman, aged 34 years, had very low visual acuity.

External eye examination showed a slight microphthalmia with normal reflexes and motility. Ophthalmoscopic examination of the right eye showed an extensive area of excavation, about 1.5 disc diameters, with a typical vascular distribution. An excavation in the left eye was about 3.5 mm. deep and 0.5 disc diameters in circumference. The blood vessels came out from this area in irregular form.

After reviewing the different pathogenic theories and affirming that those presented by von Szily and von Hippel are most plausible, the author discussed the different opinions on hereditary deformations of the fetal cleft. Since the case presented lacked information about the familial antecedents the various hereditary possibilities were taken up: (1) That it is transmitted as a recessive characteristic; (2) that it is a mutation; (3) that it is transmitted as a dominant characteristic.

He arrived at the conclusion that the most likely explanation is that the condition is dominant in incomplete form as held by Timofeef-Ressousky and Kroening, and can occur, as Curtius says, in what is called "skipping of a generation."

With respect to treatment medical ethics prescribe that the ophthalmologist follow the usual rule with reference to advice on eugenics.

Discussion. Dr. F. Galindez Iglesias: First, I want to thank Dr. del Rio for his very fine paper. Of the two fundamental types of coloboma of the optic nerve, the true coloboma arises from a disturbance in the closing of the peduncular cleft, and the coloboma of the entrance of the optic nerve is the designation given by von Hippel to the colobomatous malformation of the papilla and its surroundings. This nomenclature has merit in that it indicates the place of the malformation. It does not prejudge the nature of the affected part.

Morax called attention to the existence of excavations in these cases which at times looked like glaucomatous excavations as in the case just presented. The progress in embryology has led to a new explanation of numerous malformations—to a so-called "organizational center" which supervises the normal formation of the organs.

Speman has referred to the "organizational center" as a group of cells of particularly active metabolism, having the power to induce and organize the cellular elements. It is understandable that lesions and intoxications of this "organizational center" will produce abnormal developments which would lead to malformations.

I want to clear up the etiologic genesis of the coloboma, something that is generally more difficult than the morphologic genesis which is based on a minute anatomic examination. The etiologic genesis can result from inflammations, toxins, abnormal compressions (sometimes by the amniotic membrane), as well as by the action of X rays on the pregnant uterus which disturb the multiplication of the embryonic cells, especially those sensitive to X rays. For this reason I want to ask Dr. del Rio if there was any such treatment in his case during pregnancy. Finally, I want to point out that a congenital anomaly has the double aspect of congenital malformation and disease.

Congenital malformation is a fault of nor-

mal formation at birth and usually remains stationary, while congenital disease may appear at birth or at a later stage of life and is generally progressive. Colobomas would therefore, appear to belong to the first type.

Maranon called attention to the great frequency of congenital anomalies associated with endocrine disturbances and particularly with those of the hypothalamus and hypophysis. Babbes advanced the idea that there is a "eutrophic center" located in the hypothalamus, disturbances of which could bring about these anomalies.

Dr. Marin Amat: I also believe the designation coloboma of the optic nerve is inappropriate because it is not a case of a defect of the papilla, for the nerve fibers persist in the colobomatous excavation. But it is a depression, a true ectasia of the sclera, which is most prominent behind. In reality it is the choroid and the pigmentary layer of the retina which are absent and thus it is really a coloboma of these membranes because the visual retina frequently appears as if doubled up at the edge of the coloboma. The white color which we see is due to the sclerotic.

Finally, it is of great clinical interest to present the different grades of the incorrectly termed coloboma of the optic nerve:

1. Congenital conus of the papilla which, as its name indicates, is a depression in the form of a justopapillary meniscus, generally situated in the lower part, but, in a smaller number of cases, at the inner or upper part. It can be differentiated from the myopic conus which is always temporal, and is acquired during life, although in both conditions the refraction of the eyes may be myopic. Another difference is that the congenital conus almost always is found in amblyopic eyes, and after birth.

In congenital conus, the optic nerve emerges obliquely from the eyeball (oblique implantation). There is also a fundamental difference in the appearance of the central vessels of the retina in the congenital conus from that of the myopic conus. In the congenital, the physiologic excavation of the papilla does not have the form of a funnel but rather that of a depression in the form of a gently sloping ramp, whose upper edge is perfectly sharp as if cut with a pickaxe, while the lower border is imperceptibly lost. Thus, those vessels which go upward are obliged to describe a curve in the form of a hook in order to overcome the difference of levels; while those which go below follow the gentle slope of the conus and are visible for the whole course on the ectasia, unless this is as deep as in the second type of these malformations.

2. The coloboma properly called coloboma of the optic nerve has been excellently explained by the chairman.

3. A hole in the papilla—that is, the congenital anomaly—is characterized by the presence of a little black spot in the papilla which may be in the center or more frequently on the side. Generally, this spot is very small, but it may occupy a quarter or a third of the papilla. It is intensely black and sometimes seems to start 2 or 3 mm. from within the thickness of the optic nerve. Sometimes it is in communication with the veins of the nerve, as in the case of Seefelder. It is a very rare anomaly and such a case may not be seen in a practice of half a century.

It is most probable that the three types follow the same etiology—a defect in closing of the embryonal ocular cleft which continues its course in the anterior portion of the optic nerve. Thus the congenital conus, the coloboma of the optic nerve, and the excavation of the papilla are different grades of the same congenital anomaly and occur with a frequency corresponding to the order of their listing.

Dr. del Rio (in closing) thanked Dr. Galindez Iglesias for his fine discussion and continued: The possibility of a remote action of X rays in the case presented could not be investigated. The patient, of low mentality, has not been able to give a good history of the case, nor any details of her life or facts previous to her birth. However, we do not believe that there have been such influences.

I fully agree with the classification of con-

genital malformations and diseases. This case belongs to the first group, to the malformations. These appear at the first moment of birth, while diseases show themselves later, as occur in abiotrophies, for example.

With reference to the theories advanced by Dr. Galindez I think, as Fleischer says, in "Erb-Leiden des Auges" published in Leipzig, 1938, that the alterations in the closing of the fetal cleft are due to changes in the genes in the earliest stage, without any external or internal influences. With reference to the influence of the higher centers—hypothalamus, and so forth—I do not know very much about the studies of Dr. Maranon on the subject but I believe that the first thing to clear up is which comes first in development. I believe that malformations of the cleft are due to changes in the genes. Many times malformations of a whole system occur, as in the syndrome of Marfan.

I want to thank Prof. Marin Amat for his discussion. I have been for a long time in accord with his classification of the colobomas. The fibers of the optic nerve are spared, as Dr. Marin Amat has said, and proof of this is shown in the case of Parsons (Duke-Elder) in which it is seen that the coloboma affects the choroid immediately around the optic nerve, and this appears withdrawn in the vaginal space on the side of the coloboma. The vaginal space on the coloboma is very much enlarged and the fibers of the optic nerve are pushed back but they are not affected by the process. The papilla is variable and the vessels come out in a normal position. This is a classic example of coloboma of the optic nerve.

Basilar lordosis of Bartoletti

Dr. Mario Esteban presented a case of the basilar lordosis of Bartoletti. Of the different types of cranial dysostosis perhaps the most interesting to the ophthalmologist are deformations of the base of the cranium. The morphologic aspect of the cranium may be normal or almost normal and yet radiography will show a sinking in of the sphenoids and of the sella turcica which damages the whole bony architecture. It is in these cases that the optic nerve is most gravely and seriously affected.

The patient, a boy, aged three-and-one-half years, of normal birth, had no hereditary or familial findings. At the age of two-and-one-half years, an elevation appeared in the region of the anterior fontanelle. Later, there was slight exophthalmos, divergent strabismus, and progressive loss of vision. A month ago he began to have nystagmus, headaches, and mild vomiting.

The clinical examination showed a well-developed boy with no malformations of other parts of the skeleton. There was no syndactilia. The cranium showed a high dome and along the mesofrontal line a bony ridge could be felt rising upward like the crest of a helmet. The face showed adenoid facies, a straight nose, no prognathism, moderate exophthalmos, a divergent, concomitant strabismus, nystagmus with small oscillations, and a slight hypermetropia of less than one diopter.

The fundus in both eyes, but more marked in the right, gave a picture of optic atrophy, postneuritic or postedematous. The papillas were gray and large, with an irregular and slightly elevated contour. The arteries were narrow; the veins, not much dilated, arched on reaching the papilla and continued in a rapid, zig-zag fashion.

Pupillary light reflexes were present, although they were slow on direct stimulus, especially in the right eye. The child's age did not permit measuring visual acuity nor the visual field. Occasionally there are slight horizontal nystagmoid movements of the head.

Radiologic examination by Dr. Ortega showed: (1) A synostosis of all cranial sutures except the occipital; (2) intracranial hypertension—many and marked digitlike impressions with bulging and thinning of the frontal and parietal bones (clinical manifestations were headache, vomiting, and the appearance of the optic discs); (3) there was no separation of the sutures but there was a bony formation along the mesofrontal line

(the synostosis had converted the cranium into a rigid and inextensible box in which the growing brain could not expand); (4) a marked sinking of the sphenoid and of the sella turcica, with the sphenoidal angle of Weckler much enlarged and the middle cerebral fossa large and deep below the level of the anterior cerebral fossa; (5) the orbital cavities were short and narrow posteriorly which led to the exophthalmos and divergence of the eyes; (6) the optic foramina were triangular, flattened from above, more marked on the right, the side of the greater optic atrophy (perhaps they were also narrowed).

The papillary atrophy, either postneuritic or postedematous, could be attributed to cerebral compression or to strangling of the optic nerve by a narrow or flattened bony canal. The nystagmus was due to the amblyopia. It could also be explained by vestibular or cerebellar disturbances caused by the faulty formation at the base of the cranium.

Dr. Mario Esteban then reviewed the various pathogenic theories of dysostosis and spent some time considering the endocrine and metabolic influences which can produce hypoplasia of the cranial base, provoking or favoring early synostosis of the sutures. In this case there was hypercalcemia and phosphoremia. In the beginning, the cranial deformation was attributed to rickets and calcium and vitamin D were administered in large quantities which, although not a direct cause, might have hastened the synostosis.

With reference to treatment, one should pay attention to the nose and throat affections which in some cases have an influence. One should also study in every case the endocrine and metabolic conditions. Decompressive operations may consist of: (1) Lumbar puncture which may have only a temporary effect and is, moreover, dangerous; (2) trephination, which is said to give favorable results with a regression of the papillary edema; (3) puncture of the corpus callosum (cases are reported in which the headaches disappeared and vision became better; others in whom the operation failed); (4) resection of the roof of the optic canal either by the orbital route (Hildebrand, Worms, and Carrillon) or by transfrontal route (Clovis, Vincent). This would be the operation indicated in order to free the nerve in cases of stenosis. It is well understood that the results of the operation would be most favorable when done early to avoid atrophy of the optic nerve.

Cauterization in Scleritis and Episcleritis

Dr. Marin Amat read a paper on heat cauterization in the treatment of scleritis and episcleritis. He reviewed the local and general medications used in the treatment of inflammations of the sclerotic. He also discussed the small surgical interventions employed (subconjunctival injections, scrapings, and so forth) and the physical agencies applied, such as heat, diathermy, short-wave, radiotherapy, which generally fail or give but slight and uncertain results.

Spurred by the success obtained by Jensen, who employed heat cauterization by means of a sharply pointed cautery and obtained cures, Dr. Marin Amat began to use this form of therapy and has obtained rapid and perfect cures in a large number of cases.

He employs a cautery which is thinner and sharper than those ordinarily used in ophthalmology. The inflammatory focus in the sclerotic is first anesthetized by means of cocaine crystals; this produces absolute anesthesia so that the lids can be separated with the fingers and as many small punctures as desired can be made.

Discussion. Dr. Carreras Matas: In my opinion, in addition to the products of destruction, resulting from the small number of cells destroyed by this procedure, which excite cellular proliferation and repair, there also supervenes an axon reflex which causes a stimulation to the immediate collaterals, liberating histaminelike substances that cause a vasodilatation and thus provide better nutrition to the affected zone.

Joseph I. Pascal,
Translator.

AMERICAN JOURNAL OF OPHTHALMOLOGY

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THE AMERICAN OPHTHALMOLOGICAL SOCIETY MEETING

The 86th annual meeting of the American Ophthalmological Society was held in Hot Springs, Virginia, May 31 to June 2, 1950. The president, Parker Heath of Boston, was in the chair. There were 112 members and 18 guests registered. Nineteen papers were presented, and the general expression of opinion indicated that the program was one of the best ever given.

Burton Chance and his committee arranged a celebration in honor of the invention, 100 years ago, of the ophthalmoscope by Helmholtz. This consisted of a splendid exhibition, covering the period 1850-1865, of ophthalmoscopes, manuscripts, books, and other material relating to Helmholtz, loaned by the Army Medical Museum and individuals, under the direction and supervision of Dr. Chance, Dr. Ruell A. Sloan, curator of the Army Medical Museum, and his able assistant, Helen R. Purtle. The exhibit, skillfully displayed, was the center of attraction during intermissions and when the scientific meeting was not in session.

Dr. Chance, in a formal presentation, discussed the "Early years of Helmholtz," and delightfully sketched his early life and career, his personal characteristics and appearance at the time of his invention.

Dr. Arthur J. Bedell presented a valuable historical paper, "The first 10 years of ophthalmoscopy, 1851-1861." His description of the early reactions to the invention of the ophthalmoscope by those who thundered against the serious damage to the interior of the eye by the focusing of a "strong" light from candle or gas light, was most amusing. He very ably traced the rapid evolution of ophthalmoscopy during the first 10 years following its initiation, and concluded by pointing out the elevated stage this science occupies today.

The scientific papers covered a wide variety of topics, as is usual. Lloyd and Levitt reviewed the problem of "Endothelial dystrophy: Congenital, familial, and idiopathic," with particular emphasis on the Fuchs's type, adding several cases of congenital and familial origin to this group.

Cogan, Martin, Kimura, and Ikui described their experiences in a recent survey done by them of atomic-bomb survivors in Japan, under the auspices of the National Research Council, Committee of Ophthalmology. Eighty cases of radiation cataract were encountered in their work.

Scheie and Frayer, in a paper on "Ocular hypertension induced by air in the anterior chamber," pointed out the danger of this event and by clinical and animal experiments demonstrated that the mechanism lies in the ball-valve action produced in the eye by the air bubbles pressing the iris and pupil against the lens, thus blocking off the posterior chamber.

Kronfeld and McGarry described "The mode of action of iris-inclusion operations." A very ingenious and valuable study indicates true filtration even when there is no apparent bleb. On the other hand, DeVoe, in a careful gonioscopic study of cases in which fistulizing operations had been performed, described a number of them in which there was no visible (gonioscopically) interior filtration scar. In some of these cases, the ocular tension was controlled. DeVoe concluded that these studies tend to confirm the opinion of those who believe that the control of glaucoma is not primarily the result of mechanical fistulization. Chandler concluded in his paper on "Malignant glaucoma" that the extraction of the lens, even if not cataractous, in such an event is curative.

Woods's paper on the "Clinical and experimental observations of the effects of cortisone and ACTH in ocular diseases" was masterful. His experimental studies, in his opinion, would indicate that the remarkable changes produced by the drugs are not due to the blockage of the anaphylactic and allergic reactions present, but rather that they stop cellular and tissue response to inflammatory stimuli in some fashion hitherto unknown. Woods's paper is most significant and will appear in full in an early issue of the JOURNAL.

Cowan, in a delightful essay on "Emmetropia," reaffirmed his opinion that there is such a thing in spite of the belief of some to the contrary.

Gundersen discussed "Ophthalmia nodosa," and described a case illustrating the pathologic conditions found in his patient, with numerous and beautiful Kodachrome slides of the histologic preparations. His illustration and description of the offending caterpillar, Isia isabella, succeeded in endowing this creature with a most colorful personality.

Harrington, in a most important contribution, demonstrated the "Dynamics of phakoerisis" by means of his modified Bell erisophake. His slow-motion picture of the way the erisophake works was beautiful to see and easy to understand.

Post and Stickle discussed the "Fundus changes in juvenile diabetics" and thoroughly surveyed about 40 cases of this condition. This paper and that of Beetham on "Diabetic retinopathy in pregnancy" supple-

mented each other, and gave additional support to the belief that it is the most careful control of diabetes rather than the duration of the disease that is the essential element in the prevention or at least the postponement of retinopathy.

Fry described an unusual type of bilateral familial crystalline dystrophy of the cornea.

Von Sallmann beautifully demonstrated the early lens changes that occur in experimental X-ray irradiation of the eye. His paper was decidedly one of the highlights of the meeting and was most timely in its bearing on atomic injuries to the lens.

Vail discussed the problem of foreign materials getting into the anterior chamber during intraocular surgery and emphasized that free, floating lint in the operating room should be included among them.

Castroviejo described several cases and his technique of performing total penetrating keratoplasty, as a preliminary report. It revives interest in this procedure that had fallen into discard.

Town and Rakoff's paper on the "Relationship of the endocrines to cataract" was most thought provoking. It had to do chiefly with cataracts that occur in relatively young persons and that are produced by metabolic and endocrine dysfunction.

The Howe Medal for distinguished service to ophthalmology was awarded to Algernon Beverly Reese for his important ophthalmic scientific contributions and for his devotion and service to our science. The justice of this award to Dr. Reese was fully demonstrated by the warm and sustained applause by the members.

Dr. John H. Dunnington of New York was elected president, and Dr. Lawrence T. Post of Saint Louis, vice-president of the society. Dr. Maynard C. Wheeler of New York was reëlected secretary.

The next meeting of the American Ophthalmological Society will be held at the Greenbrier, White Sulphur Springs, West Virginia, on June 7, 8, and 9, 1951.

Derrick Vail.

ANNO MIRABILE, 1850

Although the present half-century is mathematically adapted to historical perspective, the year 1850 is a special milestone for ophthalmology since, in December of that year, Helmholtz invented its most revealing instrument, the ophthalmoscope. As Shastid said, there are just two kinds of ophthalmology—that which came before and that which followed after Helmholtz's discovery. The apparatus was rapidly simplified and improved, and, in 1852, Reute introduced the added technique of indirect ophthalmoscopy. A vast new domain was opened for exploration and in rapid succession the following discoveries were described by keen observers: In 1853, pigmentary retinopathy (Donders) and detachment of the retina (Coccius); in 1855, the cupped disc of glaucoma (von Graefe) and thrombosis of the central retinal vein (Liebreich); in 1856, hypertensive retinopathy (Heymann); in 1858, syphilitic retinitis (Jacobson); in 1859 and 1860 embolism of the central retinal artery and choked disc (von Graefe); and in 1861, optic atrophy (Ed. von Jaeger).

The scholarly T. Wharton Jones, who made some fine drawings for the later editions of Mackenzie's famous book and later contributed a celebrated text of his own, wrote in 1854: "Dr. Helmholtz, of Koenigsberg, has the merit of specially inventing the ophthalmoscope. It is but justice that I should here state, however, that seven years ago Mr. Babbage showed me the model of an instrument which he had contrived for the purpose of looking into the interior of the eye. . . . This ophthalmoscope of Mr. Babbage, we shall see, is in principle essentially the same as those of Epkens and Donders, of Coccius and of Meyerstein, which themselves were modifications of Helmholtz's." Yet Jones still minimized its value: "The little help which the therapeutics of the eye has as yet derived from the ophthalmoscope appears evident." His confrere, Dixon, was even more disparaging: "If the praise bestowed upon this instru-

ment be allowed to go forth to the professional public without strong cautions and limitations, dangerous results are likely to ensue."

In 1851, London had the first great national exhibition. While visiting it, Donders met Bowman and Albrecht von Graefe, and forthwith the trio inaugurated a lifelong friendship. Bowman, aged 35 years, had just described the limiting membranes of the retina and, in 1847, had independently discovered the meridional and radial fibers of the ciliary muscle. Von Graefe, then 23 years of age, had been studying with Arlt in Prague, with Sichel and Desmarres in Paris, with the Jaegers in Vienna, and was now revisiting London after finishing with Critchett and Bowman. Donders, although 33 years of age and already a renowned professor of anatomy and physiology, was so impressed by their fervor that he devoted himself henceforth zealously and exclusively to ophthalmologic investigation. Von Graefe had returned to Berlin the previous year (1850) and was immediately successful. He was one of the first to employ the ophthalmoscope, about which he had no inhibitions, exclaiming: "Helmholtz hat uns eine neue Welt erschlossen!"

The first American to practice ophthalmology exclusively was Henry W. Williams, who had obtained his study and training in Paris, Vienna, and London. Shortly after his return he became remarkably active in his specialty. In 1850, when aged 29 years, he was privileged to give at Harvard the first course of lectures in ophthalmology in America; was appointed the first ophthalmic surgeon of the Boston Dispensary; and translated Sichel's work on *Spectacles*. He was probably the first to employ etherization as a general practice in cataract extraction, and the first to suture the corneal wound in this operation.

In 1850, among the men about to enter ophthalmology, were Adolf Weber, who became the most adept surgeon among von Graefe's students and received all the latter's instruments as a legacy, and Jonathan Hutchinson, who was to disprove eight years later von Graefe's mistaken idea that the cornea was never affected by syphilis. In the wave of the future were Holmgren, aged 19 years, and Hering and Snellen, both aged 16 years; still in the grammar grades were Argyll Robertson (13), Javal (11), Stilling (8), and Hirschberg (6). Priestly Smith was a promising lad five years of age; Schiøtz was in diapers; and Ernst Fuchs, just a gleam in his father's eye.

The beginning of the nineteenth century marked a renaissance in medicine that reached a crescendo at midcentury. Virchow's *Cellular Pathology* had been in circulation four years; Henle's *Miasmas and Contagias*, just published, first clearly stated the concept of contagion. Though the primary etiology of disease was still attributed to climactic factors, the temperaments, and above all, the diatheses, Pasteur, now aged 38 years, was shortly to provide a truer insight. Most articles concerning the eye were published in general medical journals, some of which are still flourishing, such as the *Lancet*, the *Boston Medical and Surgical Journal*, and the *American Journal of Medical Sciences*. The last-named journal was founded by the first of our distinguished ophthalmologist-editors, Isaac Hays, who continued as staff surgeon of the Wills Eye Hospital from its founding in 1834 till 1854. Though the *Annales d'Occulistique* made its appearance in 1838, being the oldest eye journal in continuous circulation, it was only after 1850 that two more were established—the *Archiv für Ophthalmologie* by von Graefe in 1854, and the *Royal London Ophthalmic Hospital Reports* in 1857.

Before World War I, America had eight ophthalmic journals, the only ones now surviving being the *Archives of Ophthalmology*, dating from 1869, and the AMERICAN JOURNAL OF OPHTHALMOLOGY, begun in 1884. With American contributions to ophthalmic research steadily mounting, a third journal is now urgently needed, and the most valu-

able long-range benefaction that could be made in this present midcentury would be the subsidy to an "American Journal of Investigative Ophthalmology."

James E. Lebensohn.

OBITUARY

MANOEL A. DA SILVA

Manoel A. da Silva died unexpectedly on March 5, 1950. A member of the modern Brazilian ophthalmological generation, Manoel A. da Silva, although still a young man, was well known not only in São Paulo, but in Brazil and the Americas.

Born in São Paulo, he attended grade school and high school in his native city. Registering in 1933 at the Escola Paulista de Medicina, he was graduated with the first class graduated by that school in 1938. His spirit and capacity for work and organization helped him to make friends among his colleagues and it was these same qualities which aided his advancement in his professional career.

During his last year at school, he worked as monitor in the Ophthalmological Clinic of the Escola Paulista de Medicina and was afterward appointed assistant and instructor, helping not only with the teaching of undergraduates but also with graduate and postgraduate training in ophthalmology.

When the Kellogg Foundation scholarships of the Pan-American Association of Ophthalmology were established, Manoel Silva was classified in first place among the Brazilian candidates and spent a year at the Illinois Eye and Ear Infirmary at the time when Harry Gradle and Peter Kronfeld were teaching there. Later he visited several other clinics in the United States. When the Society of "Kellogg Fellows" was founded, Manoel Silva was elected president.

He was president of the Centro de Estudos de Oftalmologia de São Paulo and vice-president of the Sociedade de Oftalmologia de São Paulo. He read the official paper at the 4th Jornadas Brasileiras de Oftalmologia in Porto Alegre and had been chosen by the Sociedade de Oftalmologia de São Paulo and by the Centro de Estudos de Oftalmologia to present the official paper of these societies at the Pan-American Congress of Ophthalmology. He was one of the assistant editors of *Ophthalmologia Ibero Americana*, which owes a great deal to Manoel Silva for his tireless labor. He cooperated enthusiastically in the organization of the *Bulletin of the Centro de Estudos de Oftalmologia* and always entered wholeheartedly into all the activities of the Ophthalomological Clinic of the Escola Paulista de Medicina.

In memory of the assistant executive secretary of the Pan-American Association of Ophthalmology, a position held by Manoel A. da Silva since 1948, the Pan-American Congress of Ophthalmology, held in Miami Beach, paid a significant tribute to him, thus showing the sorrow of all ophthalmologists of this hemisphere for his premature decease.

Moacyr E. Alvaro.

BOOK REVIEWS

VISUAL DEVELOPMENT. By J. H. Prince. Baltimore, The Williams & Wilkins Company, 1949. Clothbound, 418 pages, 160 illustrations, 30 color plates. Price, $9.50.

This book is a fitting companion piece to Walls's *The Vertebrate Eye* and Polyak's *The Retina* to which the author refers occasionally in the text, giving credit to these authors, accepting them as sources of material as having investigated many of the subjects discussed in his book more fully than he. This volume is extremely readable and informative about the development of sight. Many beautiful halftones and good diagrams, as well as a few color plates of the fundi of various animals, amplify the text.

There are five parts, the first having to do with such subjects as the structure of the retina in man and in animals and a descrip-

tion of its function and method of action. The second and longest part is concerned with the evolution of invertebrates and vertebrates; their nocturnality and pupillary function. The third part has to do with color vision, the fourth with night vision and dark adaptation, and the fifth with methods of examination and a discussion of fundus significance.

The chapter on perception gives, among other things, a brief outline of the brain areas utilized for the various senses from the lower animals to man, showing the decrease in areas, the functions of which, such as smell, become less and association areas become greater the more advanced the evolution. The chapters on retinal structure are somewhat detailed for the lay reader, but elementary in comparison to the exhaustive treatises of Polyak and others.

The two sections on evolution of invertebrates and vertebrates make fascinating reading as do the following on experiments in nocturnality and diurnality.

After detailing the progressive changes in the eyes from unicellular organisms with only an eye spot through compound eyes and multiple eyes and ending with some consideration of the pineal eye, as in the surviving sphenodon, the author passes to the discussion of the general evolution from the cyclostomes, which are like parasites, through the elasmobranchii and the lungfish to the amphibians.

Amphibious life was occasioned by an attempt by smaller fish to escape from larger sea monsters. At the same time some fish sought escape in the deepest and darkest waters. Each of these changes was accompanied by suitable adaptations of body and eye structure.

Gradually the fish developed legs to replace the fins, and reptiles ruled the land. But again, the little must escape from the big and this was done by taking to the air or burrowing into the ground. And thus, the birds and snakes were born.

The birds' eyes became exceedingly efficient for their purpose, developing great visual acuity and, in some cases, double maculas to protect them from enemies in the air and to enable them to have vision for acquiring food. The snakes, having special use for vision in the dark, acquired eyes suitable for this purpose, sacrificing something of diurnality. For some unknown reason reptiles, especially the larger ones, almost disappeared from the earth and the day of the primates slowly dawned.

The countless eons, estimated by Prince at three billion years, necessary for these changes from organic solutions to modern man to take place are almost inconceivable. If we tentatively accept the estimates of physicists that there are only about 10 million years of solar energy remaining in our sun and it has taken three billion years to get us to our present stage of development, one almost feels that there is very little time left!

Pupillary function with its adaptation to life's necessities is well told. The description of the use of color in the animal world for protection and for the hunter makes another excellent chapter. The part on color vision is somewhat unsatisfying for the reason that the subject is so little understood. Many of the current theories are given, but one is left in the usual doubt as to the correct explanation.

A good chapter is that on nystagmus. The analysis of the differentiation between the congenital and acquired types is clear. The care and handling of animals for the routine examination of their eyes gives some technical information that is valuable.

In summary, this book is well written and interesting. It is by no means an exhaustive treatise on the subject and scarcely sufficiently detailed for a reference text. Both ophthalmologists and lay readers will enjoy it, there being only a few chapters that would be obscure to the latter because of lack of a medical background.

Lawrence T. Post.

THE PLACE OF THE ANOMALOUS QUOTIENT BY COLOR VISION EXAMINATION AND BY EVALUATION OF COLOR ABILITY. By Georg W. Keyser, former chairman Oslo Ophthalmological Society. Oslo, A. W. Brøggers Boktrykkeri A/S. Paper binding, 4 figures, 1 colored plate.

The anomalous quotient is obtained from tests on anomaloscopes by dividing the green-red ratio of the color deficient by that of the normal individual. This quotient gives a simpler and more exact expression than the Rayleigh equation and is independent of the quality and quantity of light employed. The author speaks well of the latest improvement of the pigment-anomaloscope of Kettesy which permits measurements with an exactitude of 0.1 mm. In deuteranomaly the anomalous quotient is about 3.6; in protanomaly, about 0.6.

The ordinary examination merely distinguishes the color-capable from the color-incapable. The anomalous quotient provides a method of evaluating color ability that can be correlated with occupational requirements. In the final judgment upon color ability, training and experience should be considered. Prospective students in the medical sciences require examination since an anomalous quotient of about 3.0 will occasion difficulty with colored titrations and the recognition of colored microscopic details.

The author's previous text, *Zur Frage der Farbentüchtigkeit*, should be read for a complete perspective of his views. The present supplemental brochure in English is generously offered gratis to American libraries and others concerned with this important subject by Dr. Keyser whose address is Øvre Slottsgate 17, Oslo, Norway.

James E. Lebensohn.

BULLETIN DE LA SOCIÉTÉ BELGE D'OPHTHALMOLOGIE. No. 91, February 20, 1949.

Hoorens discusses the anatomy and physiology of the pupillary movements. He states that the iridoconstrictor centers have a true tonus, and that the light reflex centers are located in the pretectal region and mesencephalon, and that miosis which is associated with convergence and accommodation is due to nervous impulses from the diencephalon and probably also the cerebral cortex.

Heymans discusses the pharmacology of the pupillary movements. Coppez and Coppez discuss the tonic pupil, the syndrome of Adie, Horner's syndrome, Marcus-Gunn sign, and have a rather long discussion of the mechanism of drugs on these pupils.

Sourdille discusses the importance of partial posterior synechia. He mentions the desirable features of addition of adrenalin and cocaine to atropine, among which are better dilatation and disappearance of photophobia, lacrimation, and blepharospasm. He advocates iridectomy for all patients in whom the iris shows persistent adhesions, with visual decrease, and with the advent of cataractous changes, in order to diminish the number of secondary glaucomas, to favor healing, and to reduce the number of postinflammatory cataracts.

François and Descamps describe at length two types of amyotrophic sclerosis, the Charot-Maire-Tooth type, and the Dejerine-Sottas type. Pupillary abnormalities were more common with the latter type.

Weekers and Roussel discuss pupillary alterations following the retrobulbar injections of alcohol. They used rabbits, and injected 0.5 to 20 cc. of 50- to 80-percent alcohol, which resulted in mydriasis and abolition of the light reflex, due to damage to the orbital parasympathetic iridoconstrictor fibers. They say that clinically the pupillary effects are also from damage to the iridoconstrictor parasympathetic fibers which come from the ciliary ganglion.

Leeuwen describes the pupillary syndrome observed in one family of five members. It was characterized by small irregular pupils, with retention of reaction to light and convergence. Homatropine gave a very slight dilatation. He compares true myasthenia gravis with ocular manifestation of a pseudo-

myasthemia seen in Graves's disease. In the former there is a rapid disappearance of symptoms under prostigmin.

François mentions pupillary studies in cases of heterochromia of Fuchs which is a degenerative and noninflammatory change. These patients have a sympathetic paralysis.

Dollfuss describes a patient who had total paralysis of the iris due to an intraocular metallic foreign body, with vision of 7/10. Appelmans and Forez conclude that benzedrine drops do not have any curative power in keratitis or iritis. They are perhaps useful to reinforce the action of homatropine and euphthalmine.

Bennett W. Muir.

BULLETIN OF THE SOCIÉTÉS D'OPHTHALMOLOGIE DE FRANCE. 1949, Vol. 1, No. 1, pp. 1-325.

This *Bulletin des Sociétés d'Ophthalmologie de France* unites, as planned, the reports on the meetings of the Ophthalmological Societies of Paris, Est, Lyon, Midi, Bordeaux, Sud-Ouest, Ouest, and Nord. It will be published in 10 issues; eight will be devoted to the regional societies, one to the joint meeting in March or April, and one to the meeting of the Ophthalmological Society of Paris in November of each year.

The present volume contains the reports on the joint meeting in Lyon on March 14, 1948, on the meeting of the Ophthalmological Society of Paris on January 15, 1949, of the Ophthalmological Society du Nord, on January 30, 1949, in Lille, of the Ophthalmological Society du Midi on April 11, 1948, in Marseille, and of the Ophthalmological Society du Midi on June 27, 1948, in Toulouse.

Eighteen papers on various subjects were read during the session on March 14th, and in most of them heredity in pathologic conditions of the eye was discussed. J. Sédan and Mme. S. Sédan-Bauby described two young persons with a latent glaucoma that became manifest in migrainelike attacks. The glaucoma occurred in members of three preceding generations.

A. Dubois-Paulsen, P. François, and J. Miller described unusually good results from retrobulbar injections of penicillin, 100,000 units per 1.0 cc., in early stages of severe choroiditis. Vouters believes that ocular dynamometry is an important differential diagnostic help in intracranial diseases.

Considerable emphasis was given to the use of the human and animal amnion for conjunctivoplasty in fresh form as well as in dried, thinned, and autoclaved condition. The results with the fresh material were less good because it is fragile and tears easily.

Paillas praised the use of stroboscopy in neurosurgical patients with optic atrophy. J. Sédan and Mme. S. Sédan-Bauby recommend capillaroscopy of the limbus as a diagnostic help for the study of the circulation in general. In another paper they draw attention to the possible relationship of monocular high myopia to injury caused by the application of the forceps during delivery. When, because of the pressure of the forceps on the anterior part of the eye, the posterior pole bulges, it may form a locus minoris resistentiae during future life. The same authors also contribute a study on sympathetic ophthalmia restricted to the posterior segment of the eye and include three case histories.

A critical review of the effect of streptomycin in tuberculous meningitis, optical arachnoiditis, and specific diseases of the anterior segment of the eye was given by Dejean, Cazaban, Gassenc, Calmettes, Tabarty, Gavipury, Benhamou, and Foissin, who also stress the importance of disc changes in tuberculous meningitis equal in prognostic value to choroidal lesions in miliary tuberculosis.

Alice R. Deutsch.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Vukovich, V., and Schubert, G. **Fluctuations of fixation and binocular single vision.** Arch. f. Ophth. **149**:706-718, 1949.

The authors define Panum's areas as units or circles of sensation which in size and location correspond to corresponding retinal areas. As long as rays of light impinge upon these areas binocular vision produces single images. Even during strict fixation the eyes perform movements of various types. The authors study the question whether the Panum's areas in the foveal regions of the retina are correlated in size to the movements of the eyes during fixation. They compare the sizes of Panum's areas with the areas of fixation by rather simple methods and find that each area has a diameter of 5 to 6 minutes. Voluntary and reflex movements are integrated to produce images within the borderlines of functionally conjugate retinal areas. Ernst Schmerl.

5

DIAGNOSIS AND THERAPY

Carreras Matas, B. **A regulator for the illumination of the background and the test object in projection perimeters with the Belmonte illuminator, based on the principle of Rumford's photometer.** Arch. Soc. oftal. hispano-am. **10**:197-198, Feb., 1950.

The author describes a device which provides a calculated adjustment of the illumination of the background and the test object. (1 figure.) Ray K. Daily.

Deo Ridruejo, Jose M. **A model with changeable blades for a trephine for keratoplasty.** Arch. Soc. oftal. hispano-am. **10**: 137-140, Feb., 1950.

This modification was designed to increase the availability and to reduce the price of the instruments. Its essential component is a blade similar to a razor blade and sharpened as simply, which is introduced into a cylindrical handle. It contains a centering stylet and the length of the cutting edge is adjusted by means of a screw. (1 figure.) Ray K. Daily.

Pelayo Martin del Hierro, Manuel. **An improved capsule forceps.** Arch. Soc. oftal. hispano-am. **10**:76-78, Jan., 1950.

The author believes that the difficulties in intracapsular cataract delivery are due

to the instability in the separation of the arms of the capsule forceps. To standardize this separation the author adds a regulating device similar to the one on a chalazion forceps, which permits regulation of the opening before and during its use.

Ray K. Daily.

Perez Toril, F. **Tissue therapy of Filatov.** Arch. Soc. oftal. hispano-am. **10**:74-76, Jan., 1950.

The author's experience with 29 cases of retinitis pigmentosa, optic atrophy, uveitis, and eczematous keratitis, leads him to conclude that one should not become unreasonably enthusiastic about this form of therapy, nor discard it altogether as useless.

Ray K. Daily.

Selfa, Enrique. **A consideration of the lipotropic factors in ophthalmology.** Arch. Soc. oftal hispano-am. **10**:60-67, Jan., 1950.

The author reviews the literature on the physiology of lipotropic substances and their therapeutic application and describes in a general way his impressions of this form of therapy and of histiotherapy in ocular diseases. For lipotropic therapy he uses glycocoll and naphthaquinone orally. The patients treated by both methods had high myopia, chronic iritis of obscure etiology, atrophy of the optic nerve, glaucoma, and disseminated choroiditis. The results of lipotropic therapy were generally inferior to those of histiotherapy with subconjunctival implantations of placenta. The author cautions, however, against the use of histiotherapy in glaucoma because he encountered a rise of ocular tension in a case of trachoma and one of corneal leucoma treated with subconjunctival implantations of placenta. The two outstanding impressions are that histiotherapy induces a gain in weight and a general feeling of well being during the treatment, probably as a result of the action of some antiferment of a lipase which reduces the fat combustion and is a helpful last step in the operation for retinal detachment.

Ray K. Daily.

Stocker, F. W., and McPherson, S. D., Jr. **The use of beta irradiation in ophthalmology.** North Carolina M. J. **11**:65-66, Feb., 1950.

The Iliff applicator contains a radium salt and is so constructed that the alpha rays are absorbed by a Monel metal face plate. 93 percent of the rays that pass through are beta rays and 7 percent are gamma rays. Since the beta rays are absorbed by 3 mm. of tissue and only a few gamma rays are released, this applicator has been successful in treatment of lesions about the eye. The lesions treated were limbal and palpebral vernal conjunctivitis, inflamed and recurrent pterygium, pseudopterygium, corneal vascularization, sclerosing keratitis, and papilloma of the lids.

Herman Weinberg.

Stocker, F. W. **The use of anti-histaminic drugs in ophthalmology.** South. M. J. **43**: 243-247, March, 1950.

Antihistamines supposedly nullify the effect of histamine upon the cells of the body by blocking the receptor of the cell. Numerous external diseases of the eye, such as allergic dermatitis, marginal keratitis, blepharitis, conjunctivitis, vernal catarrh, and recurrent erosions react favorably in a great percentage of cases to 0.5-percent histadyl or 0.25-percent antihistine. Dramamine, 100 mg., is recommended for postoperative nausea after cataract surgery.

Irwin E. Gaynon.

6

OCULAR MOTILITY

Comber, W. **The conditions involved in the development of concomitant strabismus.** Arch. f. Ophth. **149**:562-577, 1949.

Basic factors of concomitant strabismus are 1. incomplete development of binocu-

lar vision, 2. optical differences in the eyes due to anomalies of refraction or disease, 3. lack of proportion between convergence and accommodation, 4. abnormal position of the eyes at rest. Factors causing the first manifestations are 1. in the newborn a failure to achieve the normal position due to congenital errors, 2. in the young baby the development of near vision without development of fusion, and 3. in the mature infant a loss of fusion with increased use of near range and after diseases. The permanent state results from 1. achievement of the habit of exclusion, 2. development of amblyopia, 3. development of a new retinal correspondence and 4. development of a new muscle balance.

Ernst Schmerl.

Meesmann, A. **Surgery of non paretic vertical squint.** Arch. f. Ophth. **149**:503-519, 1949.

Results of 100 myectomies of the inferior oblique muscles are reported. A satisfactory effect following surgery of one or both obliques was obtained in 82 percent of the cases. This compares favorably with results obtained in surgery for horizontal squint. Ernst Schmerl.

7

CONJUNCTIVA, CORNEA, SCLERA

Barraquer Moner, J. I. **Results of keratoplasty.** Arch. Soc. oftal. hispano-am. **10**: 141-144, Feb., 1950.

Barraquer believes that when keratoplasty is indicated and well performed it affords excellent results. It is always successful in slowly developing lesions without iridociliary involvement, such as heredofamilial degenerations, keratoconus and disciform keratitis. The prognosis is equally good in processes with more or less iridociliary involvement which have been permanently cured, such as central leucomas that follow trauma and infection, or phlyctenular keratitis. Keratoplasty is only successful in one half of the eyes with a disease that has a tendency to recur, such as interstitial luetic or tuberculous keratitis. Vascularization, synechia and hypertension impair the prognosis to a varying extent. When transparency of the graft is not of primary importance, keratoplasty is practically always successful. Nonpenetrating kerotoplasty for esthetic purposes in blind eyes assures transparency of the transplant, and the slight cloudiness of the deep corneal layers does not affect the cosmetic effect. Thirty illustrations depict the preoperative and postoperative appearance of eyes in which keratoplasty was done for various reasons.

Ray K. Daily.

Davis, D. J., and Pittman, M. **Acute conjunctivitis by hemophilus.** Am. J. Dis. Child. **79**:211-222, Feb., 1950.

An epidemic of acute conjunctivitis occurring in the lower Rio Grande Valley of Texas was studied. The principal cause of the infection was the Koch-Weeks bacillus, although a number of attacks were caused by Hemophilus influenzae. The authors were able to differentiate the above organisms morphologically, and by fermentation tests. Some of the cases of acute conjunctivitis in this group were treated with streptomycin, and some with zinc sulfate, and the response is recorded.

Donald T. Hughson.

Garcia Miranda, Ramon. **Traumatic keratoconus.** Arch. Soc. oftal. hispano-am. **10**:51-53, Jan., 1950.

The author reports this case in support of Amsler's theory on the pathogenesis of keratoconus. A 17-year-old worker developed keratoconus of the right eye four months after the uneventful removal of a fragment of stone from the cornea. The author denies any relation between the accident and the development of keratoconus. In an examination of the left eye, with normal visual acuity, with the oph-

thalmometer it was difficult to align the mires; the author interprets this finding as indicating the presence of keratoconus fruste in the apparently normal eye.

Ray K. Daily.

Giani, P., and Foffano, L. **Lamellar keratoplasty in the treatment of trachomatous pannus.** Ann. d'ocul. **183**:216-220, March, 1950.

After a brief discussion of the advantages of partial keratoplasty, the author presents a detailed description of two cases in which the patients were greatly benefited by this procedure. A woman, 64 years of age, had a corrected vision of 0.2 in the left eye, which, after lamellar keratoplasty, increased to 0.6. A 5-mm. Franceschetti trephine was employed, and egg membrane with four sutures was used to fix the transplant. In another woman of 37 years, X-ray applications of 100 R each were used to reduce vascularization after keratoplasty. The author believes that partial keratoplasty is the operation of choice in trachomatous pannus.

Chas. A. Bahn.

Makari, J. G. **Reiter's syndrome with anaphylactoid purpura.** J. Trop. Med. and Hyg. **53**:39, Feb., 1950.

A case of Reiter's syndrome associated with anaphylactoid purpura is described. The various symptoms responded to benedryl.

Irwin E. Gaynon.

Marin Enciso, E. **Therapy of corneal cicatrices.** Arch. Soc. oftal. hispano-am. **10**:68-73, Jan., 1950.

The author advocates perilimbic subconjunctival injections of 1-percent choline for the prevention and resolution of corneal opacities in such diseases as corneal herpes, trachoma, traumatic keratitis, and in fresh leucomas that follow corneal ulcers.

Ray K. Daily.

Rabadan Fernandez, Pedro. **Bilateral band-keratitis, with disturbance in the locomotor apparatus.** Arch. Soc. oftal. hispano-am. **10**:54-59, Jan., 1950.

The author reports a case of bilateral band-shaped corneal dystrophy, involving the palpebral portion of the cornea, associated with amyotrophy of all the muscles of the lower extremities and ankylosis of the knees. The progressive character of the corneal process was followed for eight years from its beginning as a mild corneal opacity to the typical appearance of band-keratitis, more opaque peripherally than in the center and involving 3 mm. of the horizontal meridian of the cornea; the other ocular lesions consisted of posterior synechia and cataracts. The literature is briefly reviewed.

Ray K. Daily.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

D'Ermo, F. **An unusual case of lens luxation simulating an iris cyst.** Boll. d'ocul. **28**:689-695, Nov., 1949.

D'Ermo describes an eye in which, after severe uveitis, a dislocated lens caused the iris tissue to become very thin and to balloon forward so as to suggest a large cyst of the iris. (1 colored figure.)

K. W. Ascher.

Goodside, Victor. **Occurrence of acute iridocyclitis in patient having chronic simple glaucoma.** New York St. J. M. **50**:455, Feb. 15, 1950.

Acute iridocyclitis with normal tension in the right eye healed in a patient who was given 1-percent atropine sulphate and 10-percent neosynephrine solution, while a chronic simple glaucoma in the left eye reacted well to treatment with 2-percent pilocarpine. Two weeks after the inflammation in the right eye had subsided it too showed a rise in ocular tension which reacted well to treatment with pilocarpine.

Herman Weinberg.

Morax, P. P. **Etiologic study and treatment of iridocyclitis with practical deductions. Part I.** Ann. d'ocul. **183**:102-134 Feb., 1950. **Part II. 183**:161-198, March, 1950.

Not many years ago almost all uveitis was ascribed to lues and treated accordingly. Then other causes considered included gonorrhoea, tuberculosis, focal infections, brucellosis and rarer protozoal and metazoal infections, as well as metabolic diseases. Even now the etiology is not completely understood in at least 50 percent of patients. The author has made a detailed study of 252 cases observed over two years. Approximately 12 percent had clinical or serologic evidences of syphilis, 5 to 6 percent had gonorrhoea and 18 percent had focal infections. During the early stages of some diseases, such as lues and even tuberculosis, the uveitis is usually of the nongranulomatous type; in others such as gonorrhoea, the uveitis bears no relation to the duration of the extra-ocular cause. In gonorrhoeal uveitis, the anterior part of the eye is solely involved, the extraocular infection has usually been of long duration, and sulpha and penicillin therapy is seldom effective. Retrobulbar alcohol injections are suggested.

In the nongranulomatous type, the onset is usually sudden and the inflammatory symptoms are severe but the duration is relatively short. Scarring is minimal. In the granulomatous type of uveitis the onset is gradual, the inflammatory reaction less severe, but of longer duration, and nodules may exist. Fibroplastic healing begins early but frequently destroys the function of the eye. In the nongranulomatous type there are relatively few synechiae because polymorphonuclear leucocytes in the aqueous do not agglutinate as do mononuclear leucocytes. The latter form the large mutton fat precipitates observed in the granulomatous type.

In uveitis of dental origin the infected teeth are usually in the upper jaw and on the same side. X-ray pictures may not be conclusive. The ocular disease may be temporarily or permanently improved, unaffected, or even made worse by the extraction of diseased teeth. Serologic tests are of value in lues, gonorrhoea, tuberculosis and brucellosis. Polynucleosis suggests acute general infection, usually recent, and is more frequently associated with nongranulomatous uveitis. Lymphocytosis suggests chronic infection. Eosinophilia suggests an allergic factor. In sarcoidosis, anergy to tuberculin is frequent.

Chas. A. Bahn.

Morpurgo, Fabio. **Two cases of congenital aniridia.** Ann. di ottal. e clin. ocul. **75**:253-260, Aug., 1949.

Congenital aniridia is discussed at length in the light of two cases showing lenticular opacities and absence of the fovea in addition to the usual defects associated with this condition. Morpurgo concludes that ectodermal dystrophy offers a possible explanation for the various ocular defects encountered in this anomaly.

Harry K. Messenger.

Schreck, Eugen. **Clinical manifestations, microbiology and pathology of sympathetic ophthalmia.** Arch. f. Ophth. **149**: 656-679, 1949.

Because of histologic studies the author considers sympathetic ophthalmia as a condition occurring in the intraocular fluids, the cerebrospinal fluid and the lymph spaces of the bulbus, optic nerve and chiasm. A lymphotropic virus entering the uveal tract is regarded as the special causative factor. Its migration produces a perivasculitis and perineuritis. Certain histologic findings cause the author to think of the virus as a Rickettsia lymphotropica migrans. In three clinical cases a retinal perivasculitis could be observed.

Ernst Schmerl.

Sédan, Jean. **Stretching of the iris before peripheral iridectomy.** Ann. d'ocul. **183**:234-237, March, 1950.

To facilitate peripheral iridectomy the author suggests the following procedure. After the Graefe incision, the modified DeWecker scissors is introduced closed into the anterior chamber. With slight pressure against the iris the blades are opened vertically which slightly stretches the iris and flattens the pupil above. With small iris forceps and scissors a peripheral iridectomy is then performed.

Chas. A. Bahn.

9

GLAUCOMA AND OCULAR TENSION

Barreiro Saavedra, Manuel. **A preliminary communication on variations in the ocular tension during electroshock.** Arch. Soc. oftal. hispano-am. **10**:151-156, Feb., 1950.

Tonometry was done on six patients before the application of electroshock, during the coma, and several times during the period of recovery. The tension curves are uniform, and show a brusque elevation reaching its pinnacle during the coma, a rapid drop below normal and a return to the initial level.

Ray K. Daily.

van Beuningen, E. G. A. **Goniodynamometry, a test of the function of the angle of the anterior chamber in the living eye.** Arch. f. Ophth. **149**:637-655, 1949.

The author combined gonioscopy and dynamometry in the study of 16 normal and glaucomatous eyes. The outflow of the aqueous varies with different limbal zones. The speed of flow of blood from Schlemm's canal cannot be considered significant for glaucoma, but might give some hint concerning the condition of Schlemm's canal, the internal plexus and the episcleral veins. Obliteration of Schlemm's canal, sclerosis of the trabeculum and pigmentary interferences might be recognized by help of goniodynamometry.

Ernst Schmerl.

van Beuningen, E. G. A. **Postoperative gonioscopic studies of surgical procedures in glaucoma simplex.** Arch. f. Ophth. **149**: 620-636, 1949.

Five years after surgery 146 cases of primary glaucoma were studied gonioscopically. In iridectomies the normal functioning of the trabecular tissue and Schlemm's canal seem to be of greater importance than the size of the coloboma. In Elliot's trephining operation and in cyclodialysis the all-or-none law holds true. This means that if Elliot's valve regulates the ocular tension all danger seems to be prevented. However, if this valve closes, it becomes extremely difficult to control the tension by drugs. Prolapse of the iris, the ciliary body or the lens capsule into the trephined sclera favors obliteration. The results in cyclodialysis depend upon the width of the angle of the anterior chamber as well as the performance of this operation.

Ernst Schmerl.

Bonavolontà, G. **On the relation between the depth of the anterior chamber and the ocular tension.** Ann. di ottal. e clin. ocul. **75**:345-371, Dec., 1949.

In idiopathic detachment of the retina a state of hypotony usually prevails in association with increased depth of chamber. Marked hypotony and increased depth mark the presence of large or numerous tears in the retina. Normal tension and depth postoperatively point to a favorable outcome, but with persistent hypotony and increased depth the operation is more likely to prove unsuccessful. This relation between tension and depth provides a valuable prognostic criterion in those postoperative cases where a hemorrhage into the vitreous prevents observation of the fundus. In congestive

glaucoma the hypertension is in general proportional to the reduction in depth of the chamber, and the reduction tends to be greater in older subjects than in younger, and in hypermetropes than in myopes. In chronic simple glaucoma a similar relation between tension and depth of chamber occurs, though the variations are less pronounced and less constant. In infantile glaucoma the hypertension, generally of moderate degree, is accompanied by a marked deepening of the chamber in direct proportion to the degree of hypertension. In nonperforating contusions of the globe conspicuous oscillations of tension are noted and hypertensive states prevail. In general, the elevation of the tension is accompanied by a proportional increase in depth of chamber, and vice versa. In perforating injuries of the globe the initial hypotension is associated with deepening of the chamber. Persistent hypotony along with a shallow chamber is the earliest objective sign of a functional disturbance of the ciliary body that may lead to atrophy of the globe.

Harry K. Messenger.

Bottoni, Angelo. **Alterations of the iridocorneal angle in glaucoma. Gonioscopic observations.** Ann. di ottal. e clin. ocul. **75**:279-286, Sept., 1949.

The angle may be completely closed by peripheral anterior synechias (goniosynechias) or blocked by fibrosis of the trabeculum, yet all hypertensive phenomena may be absent. On the other hand, glaucoma may occur when the angle is free from synechias, when the intertrabecular spaces are permeable and Schlemm's canal is visible. The intertrabecular spaces may apparently be blocked by pigment or exudate, yet hypertension may not occur. In certain cases of uveitis a hypertensive state can occur even when the angle is wide and the trabeculum is normal. Even in the sound eye of a person with unilateral glaucoma the angle does not afford the least token whereby a predisposition to glaucoma may be recognized. There is no definite degree of narrowing of the angle that can be considered as indicating the likelihood of glaucoma. Glaucoma operations can succeed even if the angle remains closed, and may fail even if the angle is open. We can conclude that the importance of the angle and of Schlemm's canal in the genesis of glaucoma is not absolutely certain and that other factors must be investigated in the solution of the problems posed by intraocular hypertension.

Harry K. Messenger.

Carreras Matas, Marcelo. **Tonometry in induced hypertension.** Arch. Soc. oftal. hispano-am. **10**:157-165, Feb., 1950.

To determine how accurately the tonometric measurements correspond to the actual ocular tension, Carreras suggests the following procedure. The tension is taken as usual; without removing the tonometer the eyeball is subjected to a pressure of 40 grams with an ophthalmodynamometer, and the rise in the intraocular pressure on the tonometer noted. If the rise is over 30 mm. of Hg the first tonometric reading was probably too high; if it was equal to 30, the determination was exact; if it was less than 30, the tension is actually higher than that indicated by the tonometric reading. (5 figures.) Ray K. Daily.

Godtfredsen, Erik. **Glaucoma and liver function.** Acta Med. Scandinav. suppl. 234 pp. 130-135, 1949.

To substantiate Cordero's and Schmelzer's experience that about one third of glaucoma patients react abnormally to liver function tests the Takata-Ara test, thymol turbidity test, and urobilin test in urine were performed in fifty patients having glaucoma simplex. Condero and Schmelzer's work was not confirmed. (2 tables.) Herman Weinberg.

Scharf, J. **Experiences with the dia- and subscleral iridencleisis in glaucoma.** Arch. f. Ophth., **149**:586-591, 1949.

The results obtained in 40 cases are called satisfactory. Ernst Schmerl.

10

CRYSTALLINE LENS

Thompson, R. G. **Cataract with atopic dermatitis: dermatologic aspects with special reference to preoperative and postoperative care.** Arch. Derm. and Syph. **61**: 433-441, March, 1950.

Cataracta neurodermatica is an uncommon disease, the exact etiology of which is unknown, and predisposes the eye to postoperative complications. An outline of care to be given by the dermatologist is given. (2 figures.)

Irwin E. Gaynon.

11

RETINA AND VITREOUS

Damel, C. S., and Brodsky, **M. Occlusion of the central retinal vein.** Arch. Soc. oftal. hispano-am. **10**:21-34, Jan., 1950.

This is an analysis of 39 cases, relative to age, sex, fundus findings of the fellow eye, visual acuity, clinical diagnosis, blood pressure, blood urea and glucose, urinalysis, Wassermann, and electrocardiographic findings. Forty-two retinographs illustrate the evolution of the fundus picture from its incipient to the final stage of the disease. Ray K. Daily.

Owens, W. C., and Owens, E. U. **Retrolental fibroplasia.** Am. J. Publ. Health. **40**:405-408, April, 1950.

When fully developed a vascularized grayish membrane forms behind the lens and the development of the entire eye becomes arrested. When first studied, it was suggested that the membrane arose from a persistence of the embryonic tunica vasculosa of the lens, abnormal persistence of the fetal primary vitreous or from a generalized maldevelopment of both the cerebral and ocular ectoderm. The cause is still unknown but it has been shown that the disease begins in postnatal life with great dilation and tortuosity of the retinal arteries which is followed by swelling and infiltration of the retina, the development of fibrous bands in the retina which extend into the clouded vitreous and lead to extensive retinal detachment and the formation of a complete retrolental membrane by the fusion of the vitreous bands and the peripheral folds of the detached retina. It occurs in 16 percent of prematurely born infants that weigh less than 3 lbs. at birth and 8 percent of those that weigh between 3 and 4 lbs. The membrane is usually complete when the child is four months old. The first sign of degenerative change occurs when the child is four weeks old and it is not improbable that the child has by this time not only exhausted its supply of essential metabolites and, because it has difficulty in absorbing fat, does not get an adequate new supply. Metabolic studies on the postnatal course of the premature infant will probably provide a solution to the problem of the etiology of the defect and may even suggest measures for its prevention.

F. H. Haessler.

Speert, H., Blodi, F. C., and Reese, A. B. **Retrolental fibroplasia; a hazard of premature birth.** Am. J. Obst. and Gynec. **59**:246-258, Feb., 1950.

In a series of 104 white infants who were partially or totally blinded by the presence of a grayish white connective tissue membrane in the anterior vitreous, 96 percent had been born prematurely. The condition appears to be increasingly frequent and of equal incidence in both sexes. It is probable that in all monozygotic twins both are always affected but only one dizygotic twin. Genetic factors and a history of previous premature births

seem to be important in the appearance of this condition. Rubella may be a factor. (6 figures, 7 tables.)

Herman Weinberg.

12

OPTIC NERVE AND CHIASM

Ley, Adolfo. **Compression of the optic nerve by a fusiform aneurysm of the carotid artery.** J. Neurol., Neurosurg. and Psychiat. **13**:75-86, Feb., 1950.

The author reports five cases of compression of the optic nerve by a fusiform aneurysm of the carotid artery and reviews four others that have been reported. The visual symptoms appear early and are often confused with a retrobulbar optic neuritis. Cerebral angiography is useful in the diagnosis. The lesion must be differentiated from the parasellar meningiomas, the pituitary adenomas, craniopharyngiomas, gliomas of the chiasma, congenital saccular aneurysms, and opticochiasmatic arachnoiditis. The condition is ascribed to a congenital abnormality of the arterial wall. The unroofing of the optic canal and opening the dural sheaths of the optic nerves must be done as early as possible. (11 figures, 1 table.)

Herman Weinberg.

Malatesta, C. **Optic-nerve alterations in beriberi.** Boll. d'ocul. **28**:733-746, Dec., 1949.

Ten rats were fed diets poor in vitamine B_1. Controls received added vitamine. After two and a half weeks on the deficient diet, the rats showed anorexia, laziness and slower gains in weight and in 25 to 30 days ataxia, spasms, and paralyses. About one week later they died. When each experimental rat died, its control was killed; thus, rats of equal age and equal initial weight were compared. Optic nerves and chiasms were fixed in formaldehyde, embedded in paraffin and stained with hematoxylin-eosin, with Mallory's dye and with myelin stain according to the methods of Bodian and Weil. Only slight changes in the structure of the axis cylinders and in the myelin sheaths occurred in the optic nerves of the vitamine deficient animals. Varicosities of axis cylinders and granular destruction of myelin sheaths, edema, possibly increase in number of the cells of neuroglia and slight changes in capillary walls and pericapillary cells were found. (5 photomicrographs, 32 references.)

K. W. Ascher.

Mejer, F. **Papillary changes following fresh gunshot wounds of the skull.** Arch. f. Ophth. **149**:727-740, 1949.

Eighty-six cases of papilledema were observed in 282 fresh injuries of the skull. Any injury of the brain seems to produce edema and swelling. A papilledema occurring during the first 24 to 48 hours after the injury is usually caused by epidural arterial hemorrhages. Immediate surgery is indicated. Papilledemas developing at the end of the first week after the injury are signs of a posttraumatic edema of the brain. There is usually no reason for surgical interference. Papilledemas found during the second week might be caused by an inflammatory overproduction of cerebrospinal fluid, which should be studied for signs of infections. When papilledema develops during the third week brain abscess must be considered.

Ernst Schmerl.

13

NEURO-OPHTHALMOLOGY

De Leonibus, Fernando. **Pupillometric studies in vision at near.** Ann. di ottal. e clin. ocul. **75**:231-238, July, 1949.

Using the pupillometer recommended by Contino, which has a doubling device as in the ophthalmometer, De Leonibus measured the diameter of the pupils of 19 persons as they contracted in near vision.

He found that in general the contraction of the pupil in near vision does not begin until the object of fixation has reached a distance of 50 cm. from the eye, though in some subjects contraction may begin at 1 m.; the contraction reaches its maximum at 20 to 10 cm.; the reduction of the pupillary diameter averages 29 percent with an illumination of 100 lux and is independent of the refraction of the eye, except that in high myopia the pupil hardly contracts; the percentage reduction is greater the lower the illumination; age and macular changes have no effect on the pupillary reaction. Pupillometry and the nature of the near reflex are briefly discussed. Harry K. Messenger.

Urrets Zavalia, Alberto. **Congenital bilateral external ophthalmoplegia.** Arch. Soc. oftal. hispano-am. **10**:187-196, Feb., 1950.

The author reports a case of external, bilateral, congenital, nonfamilial, incomplete ophthalmoplegia, accompanied by ptosis, miosis, and pupillary rigidity. Paralysis involved the muscles innervated by the fourth and third nerves. The external rectus muscles were paretic; their partial function left the eyes in a position of extreme abduction. There was some function in the right superior rectus. The lesion is localized at the foot of the cerebral peduncles in the nuclei of the third and fourth cranial nerves. The literature on the pathogenesis of these disturbances in development is reviewed. (4 figures.)

Ray K. Daily.

14

EYEBALL, ORBIT, SINUSES

Marchesani, O. **Unilateral and bilateral endogenous inflammations of the eye.** Arch. f. Ophth. **149**:545-561, 1949.

The author feels that some information with respect to pathogenesis and etiology of certain endogenous inflammations can be obtained by studying their unilateral or bilateral occurrence. Sex and age of the patients are also considered important etiologically. A number of cases of iridocyclitis and optic neuritis serve to demonstrate his views. The involvement of the peripheral as well as the central parts of the autonomic nervous system in these conditions is emphasized.

Ernst Schmerl.

McKenzie, W. R. **Acute sinusitis with orbital cellulitis.** South. M. J. **43**:240-242, March, 1950.

Ninety percent of the cases are secondary to ethmoidal sinusitis. It complicates an upper respiratory infection. Intranasal drainage and antibiotics are indicated. (3 figures.) Irwin E. Gaynon.

15

EYELIDS, LACRIMAL APPARATUS

Angelone, Luigi. **Sanguinolent tears and Roger's cerulean disease.** Ann. di ottal. e clin. ocul. **75**:287-294, Sept., 1949.

A one-year-old child with a clinical diagnosis of interventricular septal defect was observed to shed sanguinolent tears after a severe bout of convulsive crying. The presence of serum and red blood cells in the lacrimal fluid can be explained on the basis of increased vascular permeability resulting from cardiac insufficiency and consequent stasis.

Harry K. Messenger.

Baumann, Adamo. **A rare and unusual case of functional nervous blepharospasm.** Ann. di ottal. e clin. ocul. **75**:221-230, July, 1949.

A 29-year-old teamster, unexpectedly dazzled by intense glare from the headlights of an automobile, was seized with an attack of blepharospasm which persisted two days but was promptly and completely relieved by suggestion. The

eyes were normal, but the patient was obviously hypersensitive and hysteroid.

Harry K. Messenger.

Beiras Garcia, A. **A preliminary report on dacryoscopy.** Arch. Soc. oftal. hispano-am. **10**:35-46, Jan., 1950.

The author is devising a dacryoscope, similar to a urethroscope in design, for the inspection of the anastomotic opening between the nose and lacrimal sac after dacryocystorhinostomy. Such direct inspection of the operated area will enable the surgeon to see the postoperative process, and to find the causes of failure. It will expose to view and facilitate management of scars, polyps and granulations blocking the opening. In cases of occlusion of the opening by a cicatricial membrane, it may be possible to incise this membrane with the cautery or with diathermy under direct inspection, avoiding the necessity of re-opening the external incision. (6 black and white, 4 colored figures.)

Ray K. Daily.

Djacos, Constantin. **Canalicular contamination in trachoma.** Ann. d'ocul. **183**: 135-141, Feb., 1950.

This complication is more frequent than one would infer from the literature; 37 percent of trachomatous patients show functional or structural involvement of the canaliculi. This is usually associated with other cicatricial changes such as pannus, entropion and trichiasis. The upper canaliculus is more frequently involved and the condition occurs more often in those who have been imperfectly treated. Canalicular involvement is of special importance if intraocular operations are contemplated. Secondary infections are not infrequent. The generally accepted treatment is pressure or dilatation with irrigation, in more severe cases sac extirpation. Four illustrative cases are described.

Chas. A. Bahn.

Kendig, E. L., Jr., and Guerry, DuPont III. **The incidence of congenital impatency of the nasolacrimal duct.** J. Pediat. **36**:212-213, Feb., 1950.

These investigators previously had reported the incidence of impatent nasolacrimal ducts in a series of 200 unselected full term infants as 6 percent. The present paper gives an incidence of 5.7 percent in 1,000 unselected new born infants. The diagnostic criteria for the condition were the presence of epiphora and of mucopus after pressure over the lacrimal sac. It was found in the first 200 cases in which there was a satisfactory follow-up that the vast majority cleared under conservative treatment with penicillin ointment, locally administered. The authors advise probing of the nasolacrimal duct under general anesthesia when this procedure is necessary.

Donald T. Hughson.

Marin Amat, M., and Marin Enciso, M. **The latest improvements in dacryocystorhinostomy.** Arch. Soc. oftal. hispano-am. **10**:48-50, Jan., 1950.

The authors found on reoperation that failure after dacryocystorhinostomy is frequently due to occlusion of the anastomotic opening between the lacrimal sac and the nose by adhesions between the posterior and anterior flaps, when two flaps are sutured, or by adhesion of the simple flap or the opening of the canalicular junction to the borders of the osseous opening. To avoid these adhesions Marin Amat formerly described a suture which holds the anterior flap firmly to the skin, and away from the osseous opening. Further insurance against adhesions consists in placing the osseous opening high and far back; this, however, places the surgical procedure in a highly vascularized area, which is conducive to hemorrhage during and after the operation. To check hemorrhage the authors use sulfathiozole powder, which serves as an effective hemostatic during the operation; after the op-

eration they place a gauze pack saturated with the powder against the opening in the nose, and keep the opening packed for 5 or 6 days. The external incision is made through the skin and subcutaneous tissue; the deeper structures are exposed by blunt dissection and the angular vein is tied, if encounterd. Ray K. Daily.

16
TUMORS

Cordero, Celso. **A case of papilloma of the bulbar conjunctiva and one of papillary cystic epithelioma of Redslob.** Arch. di ottal. **53**:169-202, May-June, 1949.

Two cases of papilloma in the conjunctiva are presented. The first was in a 26-year-old man who had a red, superficially ribbed nodule the size of a small chick pea in the inferior quadrant of the bulbar conjunctiva. There were four small nodules, the size of a pinhead, on the margin of the upper eyelid. It had the typical histologic structure of a papilloma. The second, in a woman of 30 years, was pedunculated, the size of a kernel of corn, red and attached to the inferomedial quadrant of the conjunctiva in the region of the semilunar plica. It was classified as a papillary cystic epithelioma of the conjunctiva of Redslob, which is characterized above all by the presence of mucus or calciform cells in the center of the mass.

Papillomata originating exclusively from the bulbar conjunctiva are extremely rare. Only 19 others have been reported. They are essentially benign, but recur.
Francis P. Guida.

Craig, W. M., and Gogela, L. J. **Meningioma of the optic foramen as a cause of slowly progressive blindness.** J. Neurosurg. **7**:44-48, Jan., 1950.

Meningiomas arising from the orbital cavity are a very small part of the intracranial meningiomas. Those starting in the optic foramen itself, tending to spread to the orbit and into the cranial cavity, occur rarely, grow unusually slowly, and are frequently bilateral. Such "foraminal meningiomas" produce a slowly progressive blindness and are not accompanied by headache or pain. Three surgically-treated cases are reported. Early recognition by field studies, followed by early removal of the tumor, has stopped the progress of the blindness. In one of the reported cases, visual improvement followed operation.
Francis M. Crage.

Fuchs, Adalbert. **Divided nevi of the eyelids.** Urol. and Cutan. Rev. **54**:88-90, Feb., 1950.

A very unusual type of nevus, which affects corresponding parts of the two lids, including the free margin, is described. When the lids are closed the nevi adjoin and appear as one. In some cases the upper and lower nevi are continuous, and are connected by an isthmus of the same growth at the canthus. The nevi are probably all congenital. Nine cases are reported. Where the nevi were not connected their presence was explained by the assumption that they started when the lids were as one during fetal life. Unless signs of malignancy occur they should be left alone. Francis M. Crage.

Hamilton, J. B. **Orbital tumours.** Australian and New Zealand J. Surg. **19**:101-108, Nov., 1949.

A survey was made of one hundred cases of orbital tumor. Twenty-seven or about 25 percent were from Tasmania and Australia. The remainder were European and American. There was a surprising incidence of orbital tumors in the first decade of life. In the Tasmanians and Australians orbital tumors were twice as common in males as in females, while in the Europeans and Americans the reverse was true. Donald T. Hughson.

Moro, Ferruccio. **Researches on the morphobiology of melanomas of the cho-**

roid. I. On the finding of nerve fibers in the intraocular neoplastic mass. Ann. di ottal. e clin. ocul. 75:239-252, Aug., 1949.

Moro reports the finding of unmyelinated nerve fibers in three melanomas of the choroid. These fibers, which presumably take origin from the ciliary nerves, have no demonstrable connection with either the cells of the tumor mass or with the blood vessels, and appear to be entirely nonfunctional. Their presence in the periphery of pedunculated mushroom-shaped tumors indicates that they are truly neoplastic and not merely pre-existent. The presence of new-formed nerve fibers in melanomas of the choroid does not seem to have been previously reported, but they do not afford a new criterion for settling the moot question of the histogenesis of this kind of tumor. (6 photomicrographs.)

Harry K. Messenger.

17

INJURIES

Callahan, Alston, **Foreign bodies of the eye.** J.A.M.A. 142:249-256, Jan. 28, 1950.

The foreign body should be localized as well as possible with the help of a strong focused light and a magnifying loupe. The vision should be obtained as soon as possible for each eye. Staining with 2-percent fluorescein helps to determine whether there is any denudation of the cornea. Study of the eye with the ophthalmoscope and the slit lamp carefully is advisable and X-ray localization by the use of Sweet or Comberg-Pfeiffer methods is recommended when possible. Intraocular foreign bodies should be removed by the anterior route when possible. If it is necessary to use the posterior route, the foreign body should be extracted through the pars plana of the ciliary body. The use of the Berman locater, the small and large magnets and the surface diathermy are discussed. (5 figures, 1 table.) H. C. Weinberg.

Cogan, D. G. **Lesions of the eye from radiant energy.** J.A.M.A. 142:145-151, Jan. 21, 1950.

Radiant energy is divided into two types. In the first type there is electromagnetic radiation represented as waves of energy which vary in length from hundreds of meters such as radio waves to thousandths of a millimicron such as cosmic rays. In the second type there is corpuscular radiation of subatomic particles such as electrons and neutrons. These have biologic effects similar to those of certain parts of the electromagnetic spectrum. They may be considered the corpuscular counterparts of the corresponding electromagnetic bands. The long radio-diathermy rays are transmitted through the eye readily without appreciable absorption and with little biologic effect. The short diathermy waves (of the order of several centimeters) induce heat effects with deleterious effect on the anterior segment. Direct current of electricity in the eye causes heat with coagulation and electrolysis. The infrared rays penetrate the transparent portion of the eye and are absorbed by pigment of the iris. The ordinary roentgen rays penetrate the eye more completely the higher the potential used in their production. The pathologic changes caused by the various rays in each section of the eye are discussed thoroughly and methods for protection are described. Prophylaxis is of utmost importance. H. C. Weinberg.

Cordes, F. C. **Emergency treatment of chemical burns of the eye.** Postgrad. Med. 7:45, Jan., 1950.

No matter what the chemical, the first thing to do is to lavage the eye copiously with water. The physician can then anesthetize the eye, inspect it and remove any solid particles which may be left in

the fornices which have not been flushed out. The alkali burns which soften and penetrate the tissues should now be irrigated with 0.5-percent acetic acid. The acid burns which precipitate the protein should be well irrigated again with water. The new refrigerants (dichlordifluormethane F 12, and dichlor-tetrafluorethane F 114) are not soluble in water but are miscible in oil, and injuries with these should be treated with repeated instillations of olive oil. H. C. Weinberg.

Grant, W. M. **Chemical burns of the eye.** J.A.M.A. **142**:152-159, Jan. 21, 1950.

The effect of any chemical on the eye varies directly with the amount of exposure and the duration of the exposure. Most of the substances react with specific groups in the tissue and alter their biologic properties. In some cases there is denaturation of substance or enzymic constituents. The depth and severity of injury is influenced by the physical solubility and the facility with which it penetrates the cornea. The solvent properties of a wetting agent or organic solvent damages by altering the physical environment. The pathology of destruction and the histology of repair of the tissues is discussed briefly. Treatment of a chemical injury is discussed with stress placed upon early copious irrigation with water.
H. C. Weinberg.

Marshall, Don. **Lacerations and perforations of the lids and globe.** J.A.M.A. **142**:246-249, Jan. 28, 1950.

Careful examination and diagnosis are important. Muscle injuries, emphysema with fracture from the nasal sinus, fracture with pressure on the optic nerve, retained foreign bodies, glaucoma and contusions, are all possible. The cornea must be protected from drying and additional trauma. It is well to keep the patient at rest until the severity of the injury is fully determined and to allay fear of blindness if possible. Fourteen conditions for enucleation are listed. An outline of repair is given with the admonition to save as much tissue as possible and to close lightly because of postoperative edema. As much bone as possible must be saved after fracture. Traumatic detachments of the retina are amenable to diathermy operations. Blood in the anterior chamber should be removed if necessary, or a miotic instilled to help prevent added hemorrhage.
H. C. Weinberg.

Payne, B. F. **Ocular contusions in national emergencies.** J.A.M.A. **142**:243-246, Jan. 28, 1950.

Contusions of the eye are nonperforating wounds caused by blows or explosions in which the fibrous tunic remains intact. The most vulnerable portion is the lamina cribrosa. It is pushed backwards and causes edema and hemorrhage into the disturbances are hemorrhage into the lids, conjunctiva, anterior chamber, vitreous, retina, and choroid. A subluxation of the lens often occurs. A disruption of the tissues with corneal edema, iridodialysis or detachment of the retina may appear. Intraocular foreign bodies must always be suspected and it is well to hospitalize the patient if the injury appears severe.
H. C. Weinberg.

Purtscher, Adolf. **Injuries of the eye by bee stings.** Arch. f. Ophth. **149**:719-726, 1949.

Twenty-six cases were observed among 67,000 patients. The importance of removing the sting is emphasized.
Ernst Schmerl.

Sellas, J. **An analysis of 414 intraocular and orbital foreign bodies with double ocular perforations.** Arch. Soc. oftal. hispano-am. **9**:1178-1201, Nov., 1949.

The frequency of intraocular foreign bodies in this series was 3.25 per thousand

injuries, of which 56.28 percent were perforations of the left eye. More than half of the foreign bodies entered through the cornea, and a fifth through the sclera; in 2.41 percent the injuries were so old and the wound so small that it was invisible.

In the diagnosis the author emphasizes the value of testing for pain with the magnet, before anesthesia is induced for the extraction. The absence of pain in the presence of a presumably magnetic foreign body, demonstrated with the X ray, is a fairly reliable indication that the foreign body is outside of the eyeball.

The gravity of the prognosis is attested by the complete loss of vision in 40.8 percent of the eyes in this series; 23.72 percent recovered with normal vision. The point of perforation is of prognostic importance; the central corneal injuries are most deleterious to vision. The three most damaging complications of such injuries are intraocular hemorrhage, traumatic cataract, and infection. From a prognostic standpoint, nonmagnetic foreign bodies are more serious than the magnetic ones. The tolerance of the eye to foreign bodies varies with their nature; copper is very irritating to the vitreous and anterior chamber, and less so to the iris, lens, and ciliary body. The tolerance for iron is similar to that for copper, except that it is tolerated better in the anterior chamber. So is the ocular reaction to nickel except that it becomes encapsulated more rapidly. Chrome is tolerated better than these metals. Zinc produces exudates in the vitreous and retinal degeneration. Lead is not tolerated in the vitreous. Aluminum, gold and silver are tolerated comparatively well. Rustless steel produces but little reaction and no siderosis. Glass is tolerated well, unless lodged in the retina, where it produces retinal degeneration. Stone is also tolerated well, and sometimes it is expelled spontaneously from the iris, lens, and ciliary body; in the anterior chamber it may cause hypopyon, which may absorb, and the stone remain there without producing further irritation. The author holds that the generally accepted belief that foreign bodies imbedded in the vitreous predispose to sympathetic ophthalmia is erroneous. Among his cases one eye tolerated a metal particle for 32 years; three had a magnetic particle imbedded in the iris, for 28, 23 and 11 years respectively. Five patients with good vision had ophthalmoscopically visible encapsulated foreign bodies in the chorioretina. In spite of these exceptional cases, the author advocates removal of all foreign bodies. Precision in localization is indispensable to successful extraction. There are no new viewpoints in the management of complications incident to trauma. Ray K. Daily.

18

SYSTEMIC DISEASE AND PARASITES

Buesa, Lorente. **A case of external ophthalmomyiasis caused by Oestrus ovis.** Arch. Soc. oftal. hispano-am. **10**:145-150, Feb., 1950.

Buesa reports a case of traumatic conjunctivitis caused by the larvae of Oestrus ovis. The patient felt a foreign body enter his eye, while unloading coal. The immediate search for a coal particle by an ophthalmologist revealed instead the moving segments of the larva in the lower fornix. Fourteen or 15 larvae were removed and the conjunctival irritation promptly subsided. The identification of the larvae was made by a parasitologist. (4 figures.) Ray K. Daily.

Burch, E. P., and Freeman, C. D. **Associated diseases of the skin and eye.** Minnesota Med. **33**:147-153, Feb., 1950.

Some of the more interesting diseases that have common ophthalmologic and dermatologic findings are presented. The authors omitted a discussion of those con-

ditions associated with systemic disease, such as syphilis and tuberculosis, and the endocrine and metabolic disturbances.

Theodore M. Shapira.

Choremis, C., and Joannidès, T. **Ophthalmoscopic observations on infants with tuberculous meningitis and miliary generalized tuberculosis treated with streptomycin.** Ann. d'ocul. **183**:221-233, March, 1950.

Repeated ophthalmoscopic examination is advised in all infants with potential tuberculous meningitis. The first evidence of the disease or its recurrence may be observed in the fundus and the ocular complications frequently are an index of the progress of the disease. Choroidal tubercles suggest hematogenous dissemination of the miliary tuberculosis because they occur in approximately one half of the cases and much less frequently in tuberculous meningitis. In the latter condition, paralyses of the third and sixth nerves and papilledema are the most frequent ocular complications. Papilledema early in the disease is considered of special prognostic importance and its appearance after treatment with streptomycin is considered a grave prognostic sign. Papilledema may also occur as an evidence of meningeal involvement in primary miliary tuberculosis. Streptomycin is considered of value therapeutically, and no toxic symptoms followed its use. The author analyzes approximately 100 cases.

Chas. A. Bahn.

Downing, A. H. **Retrolental fibroplasia.** J. Iowa St. M. Soc. **40**:60-65, Feb., 1950.

The author discusses the various theories for the cause of retrolental fibroplasia, and reviews the work of William and Ellen Owens. The history of seven children with this condition, and their ocular findings are presented.

Donald T. Hughson.

Esteban, Mario. **The radiologic syndrome of basilar lordosis of Bertelotti.** Arch. Soc. oftal. hispano-am. **10**:122-136, Feb., 1950.

A three-year-old child was apparently normal for his first two years. Then an elevation of the anterior fontanelle appeared, and the eyes became divergent; some months later he developd an ocular nystagmus, which was soon followed by a horizontal nystagmus of the head, and some exophthalmos, headache, and vomiting. The ophthalmoscopic picture was that of optic neuritis in evolution towards optic atrophy. Radiologic study, which is described in detail, revealed a premature synostosis of the cranial vault, and a picture of intracranial hypertension. The premature closure of the mesofrontal and sagittal sutures resulted in compensatory deformity at the base of the skull, designated by Bertelotti as basilar lordosis, with destruction of the sphenoids and the sella turcica. The diminished size of the orbits accounted for the exophthalmos, and their divergence for the divergence of the eyes; the optic nerve involvement is the result of intracranial hypertension, stenosis of the optic canals, and direct compression of the chiasm by the cerebrum. The nystagmus may be due to the amblyopia, to cochlear and vestibular disturbances, or may be cerebellar in origin. The literature on the pathogenesis of this anomaly and its treatment are thoroughly reviewed. For this case the author proposes a cranial trepanation, to be followed if necessary by surgery for relief of the stenosis of the optic canals. (7 figures.)

Ray K. Daily.

Ghent, E. R. **Psyche and eye.** McGill M. J. **19**:101-117, April, 1950.

Ghent not only calls attention to the use of the eye in metaphore and poetry but gives examples of the far from negligible part played by the mind in the development of styes, myopia, glaucoma,

vasomotor disturbances, oculogyric crises, asthenopia and hysterical ocular manifestations. F. H. Haessler.

Gilchrist Gibson, J. B. **Eye complications of leprosy.** M. J. Australia **1**:8-11 Jan. 7, 1950.

Ocular complications of leprosy were seen in 34 of 55 white lepers in Queensland. The frequency and severity of these lesions depend upon the duration and severity of the disease itself and also upon the type of leprosy. It is more severe in nodular and mixed types. The frequency and nature of the various ocular lesions differed considerably, in many instances, from those recorded in other parts of the world. The cornea was the tissue most affected and the commonest lesion seen was the superficial punctate keratitis which is pathognomonic of leprosy. A condition apparently not observed elsewhere was "yellow eye," a diffuse yellow coloration of previously white sclerotics, followed about six weeks later by acute plastic iritis.

Sulphonamide and penicillin therapy had no effect upon the ocular lesions. Lactoflavin, given intramuscularly, is of some value in the treatment of the superficial punctate keratitis of leprosy. Whatever immediate results are achieved by various ocular treatments, the ultimate condition of the patient's eyes depends largely upon whether or not the disease itself is arrested. Theodore M. Shapira.

Hollenhorst, R. W., and Wagener, H. P. **Loss of vision after distant hemorrhage.** Am. J. M. Sc. **219**:209-218, Feb., 1950.

Unilateral or bilateral, sudden and permanent, serious or total loss of vision following hemorrhage, usually massive and in a tissue remote from the eye, has been known for centuries. The onset of the visual loss, usually instantaneous, may be delayed for days after a single massive hemorrhage or after the last of a series of smaller hemorrhages. In Singer's series, the largest reported, the greater number occurred in females (54.6 percent); 40.2 percent of the hemorrhages arose in the gastrointestinal system and 32.8 percent were uterine. Field changes varied greatly. Many affected eyes had a normal fundus. The most common eyeground finding was ischemic optic neuritis. Retinal hemorrhages and a picture resembling that of central artery closure occur. Loss of blood is considered the ultimate cause. How this produces the ocular changes is unknown. The essential factor seems to be anoxia. The manner in which anoxia is brought about, and why it affects the retina in some and the nerves or the visual pathways in others remains unknown. The treatment is first to replace the lost blood by prompt transfusions. Duke-Elder advised paracentesis; Puppel advised immediate hysterectomy in uterine bleeding with visual loss. He reported two cases where this treatment was successful. Francis M. Crage.

Mata, Pedro. **Epiphora due to bacterial allergy.** Arch. Soc. oftal. hispano-am. **9**: 1285-1292, Dec., 1949.

Mata reports three cases of recurrent epiphora, caused by an allergy to the bacterial flora of the nose. The diagnoses were made because of the absence of organic changes in the lacrimal passages or in the nose, positive tests of allergy to the various bacteria cultured from the nose, and the therapeutic response to a desensitizing vaccine. Ray K. Daily.

Valente, Adolpho. **Some problems of psychosomatic medicine in ophthalmology.** Rev. brasil. oftal. **8**:145-171, March, 1950.

With a number of references to the literature of the subject, clinical case-reports illustrate the necessity of combining examination of the patient's refraction

and extrinsic muscle condition with study of the relationship between the eye and the patient's general physical and mental condition. The illustrative cases include several of muscular imbalance.

W. H. Crisp.

19

CONGENITAL DEFORMITIES, HEREDITY

Grignolo, A. **Two cases of congenital multiple iridocorneal adhesions, one of them connected with deformity and ectopia of the pupil (dysgenesis mesodermalis corneae et iridis, Rieger).** Boll. d'ocul. **28**:641-648, Nov., 1949.

Grignolo describes two examples of this congenital anomaly. In the one that is illustrated there are at least 20 circumscribed round or oval corneal opacities. In each opacity a strand of tissue from the iris is adherent which looks like an inverted rather thick-stemmed umbrella. They caused ectopia and deformity of the pupil. In one of the patients the lesion was present in both eyes. K. W. Ascher.

Lepri, Giuseppe. **A case of congenital malformation, ocular and extraocular (syndrome of Lohmann).** Arch. di ottal. **53**:203-221, May-June, 1949.

Lepri describes multiple congenital malformations which involved the ocular bulbs, the fingers (rudimentary supernumerary fingers) and the cranial bone (a foramina parietalia permagna). He attempts to explain the etiology.

Francis P. Guida.

Paufique, L., Etienne, R., and Bonnet, J. L. **Posterior embryotoxon of the cornea.** Ann. d'ocul. **183**:81-101, Feb., 1950.

This rare dysplasia is essentially a bilateral, mesodermal, constitutional, progressive degeneration which develops before or shortly after birth. The posterior corneal lamellae, the filtration angle, and the iris are most frequently involved, though occasionally the lens and posterior uvea are also subnormal. The corneal opacity is ring shaped, peripheral, and extends forward from Descemet's membrane. The angle of the anterior chamber is often partly or completely occluded with resulting hypertension. The iris hyperplasia is clinically manifested by color changes as in essential iris atrophy. In microscopic sections, hyalin, which is a product of degeneration, has frequently been observed in the affected cornea, filtration angle, and iris. In the differential diagnosis one considers anterior embryotoxon, congenital central leucoma, dermoids, corneal opacities with buphthalmos or tumor, as well as fetal parenchymatous opacities associated with lues and viral diseases. In some cases dominant heredity has been found to exist. The author reports two cases. The first occurred in a 14-year-old girl with divergent strabismus. Characteristic corneal opacities were observed with iris hypoplasia especially in the left eye. The lens was opaque and the iris stroma was easily transilluminated. The other patient, a 26-year-old woman, also had typical corneal opacities, dystrophic cataract and iris coloboma.

Chas. A. Bahn.

Wiswell, G. B., Marshall, C. S., and Metcalfe, D. C. **The Sturge-Weber syndrome.** Canad. M. A. J. **61**:623, Dec., 1949.

A case of the Sturge-Weber syndrome in a three-and-a-half-year-old child is reported. This patient showed four of the five criteria of the syndrome. Ocular manifestations were absent.

Donald T. Hughson.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Alcala Lopez, Antonio. **Trachoma and military service.** Arch. Soc. oftal. hispanoam. **9**:1102-1106, Oct., 1949.

The author deplores the fact that trachoma serves as an exemption from military service, and points out that numbers of young men deliberately avoid treatment or acquire the disease intentionally with the purpose of escaping service. As a result they spread contagion in their unsanitary dwellings. He suggests that instead of exempting trachomatous people, they should be concentrated in battalions and compelled to accept therapy. Ray K. Daily.

Arriaga Cantullera, Jose. **Ophthalmology in Seville in the 18th Century.** Arch. Soc. oftal. hispano-am. **10**:166-186, Feb., 1950.

The development of ophthalmology is briefly reviewed beginning with the Arabian contribution in the ninth century and five publications of Sevillian ophthalmologists of the 18th century are reviewed in detail. Interesting reference is made to the invasion of Spain during this century by a German quack whose extensive advertisements promised cures of all ocular diseases by the laying on of hands after his medicine had been applied. (*2* figures.)
Ray K. Daily.

Delthil, S., and Morel, J. **Classes for amblyopes.** Ann. d'ocul. **182**:889-925, Dec., 1949.

Although sight saving classes were first discussed by Maddox in 1884, the first class was actually begun in London during 1908. Similar classes were instituted in Strasbourg, 1911; in Boston, 1913, and in Paris during 1924. In Paris, entrants are given general physical examinations as well as an ocular examination, including refraction, and treatment if it is indicated. Re-examinations are made twice yearly. There are five schools for amblyopes in Paris, one for boys, another for girls, and three coeducational. These classes both in curriculum and in arrangements are similar to those used in this country, being adapted from the recommendations of the American Society for the Prevention of Blindness. Illustrations of the Binet-Simon test, pictures used in classes, and a special type of magnifier are presented. A graph shows the mental status of the pupils. Limited intelligence of slight degree predominates. Vocational training is emphasized in the classes.
Chas. A. Bahn.

Ophthalmic Miniature

Whether it be the gay visions that surround us in the intoxication caused by opium; the comic phantasmagoria that hashish conjures up; the compact shapes that belladonna brings so near us; the airy forms seen in our dreams, or the scintillations produced by pressure, they all proceed from irritation of the special sensory power, and it is indifferent to the brain whether it receives its impressions from direct vision, or only from internal influences.

Albrecht von Graefe, *Sight and the Visual Organ*, 1872.

NEWS ITEMS

Edited by Donald J. Lyle, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

Deaths

Dr. Harry Friedenwald, Baltimore, Maryland, died April 8, 1950, aged 85 years.

Dr. David Washburn Wells, Newton, Massachusetts, died March 4, 1950, aged 87 years.

Dr. H. Fischer-von Bünau, Bilthoven, Germany, died July 23, 1949.

Announcements

Orthoptic course

A nine-month course for the training of orthoptic technicians will begin on October 2, 1950, under the auspices of the George Washington University School of Medicine. Application should be made to Dr. Ronald A. Cox, professor of ophthalmology, George Washington Hospital, 901 23rd St., N.W., Washington, D.C.

Ophthalmologist wanted

The Public Health Service is conducting a nation-wide program on the control of chronic diseases. The conservation of vision is an integral part of this program. To this end, the Public Health Service has created the position of "Chief of the Sight Conservation Program."

The man selected will have the responsibility of developing a new type of public health program, and would have available the help and experience of men who have developed similar programs in other fields.

The appointee should be a certified ophthalmologist and will be appointed on a full-time basis either as a regular or reserve commissioned officer in the Public Health Service. The grade and remuneration depend on the age of the individual—the salary varying from $5,686 to $9,984 per annum.

Any interested ophthalmologist should communicate directly with Dr. A. L. Chapman, Public Health Service, Federal Security Agency, Washington 25, D.C.

Plastic surgery award

The Foundation of the American Society of Plastic and Reconstructive Surgery offers a first prize of $300, a second prize of $200, and a certificate of merit for essays on some original, unpublished subject in plastic surgery. Competition is limited to residents in plastic surgery of recognized hospitals and to plastic surgeons who have been in such specific practice for not more than five years.

Essays must be in before August 15, 1950. Further information may be obtained from the secretary, Dr. Clarence R. Straatsma, 66 East 79th Street, New York, New York.

Research facilities expanded

An $18,000 extension of the research laboratories of the Division of Ophthalmology at the University of California Medical School, San Francisco, has been completed. The extension provides three new research laboratories. Construction was financed by private patients treated by members of the staff of the division. One laboratory will be used in research on uveitis and a second in research on virus diseases of the eye; the third laboratory will be for studies of radiation effects on the function of the eye.

Heads Kansas eye department

Dr. Albert N. Lemoine, Jr., member of the faculty since 1947, has been appointed chairman of the Department of Ophthalmology at Kansas University School of Medicine, Kansas City. He succeeds Dr. John A. Billingsley, who is retiring because of illness but will remain active in the department. Dr Lemoine received his medical degree from Washington University School of Medicine, Saint Louis, in 1943. He was a teaching and resident fellow in ophthalmology at Harvard Medical School, Boston. Last summer he was a member of the Alaska Medical Mission, conducted jointly by the American Medical Association, U. S. Department of the Interior, and the Army Air Forces.

Societies

Mobilization to prevent blindness

On May 24th, a meeting of Mobilization to Prevent Blindness, sponsored by the American Academy of Ophthalmology and Otolaryngology and the National Society for the Prevention of Blindness, was held in New York.

Frank H. Woods, Jr., president of the Illinois Society for the Prevention of Blindness, was the principal speaker on the noon luncheon. The subject of his address was "A united effort to fight blindness."

CONDENSED CHAPTERS FROM

The History of the Guild

THE NATIONAL GUILD IS FOUNDED

The Philadelphia Guild of Prescription Opticians, founded in 1923, had hardly begun functioning before inquiries came from out-of-town opticians: "What is the Guild?"; "What does it do?"

The practical answer was to invite the inquiring dispenser to attend a meeting of the Philadelphia Guild, to find out personally.

And having attended a meeting, almost always the response was the same: "The things you discuss are the things *I* want to discuss. The things you are doing are the things *I* want to do. Isn't there some way in which *I* can join?"

But how could a man from New York, New Jersey, Delaware, Massachusetts or Connecticut become a member of a *Philadelphia* Guild?

There was only one answer, and that was the formation of a *national* organization, which took place in 1925 when the Guild of Prescription Opticians of America was formed.

The first year there were only 17 members. This Silver Anniversary year the Guild's membership is nearing 350; from the west coast to the eastern seaboard, from Canada to Florida.

There were *reasons* for this growth; reasons that we shall tell you about in later chapters of this little "history."

The Guild of Prescription Opticians of America, Inc.
110 E. 23rd Street New York (10) N.Y.

PRESCRIPTION OPTICIANS

A nine-month course for the training of orthoptic technicians will begin on October 2, 1950, under the auspices of the George Washington University School of Medicine. Application should be made to Dr. Ronald A. Cox, Professor of Ophthalmology, George Washington Hospital, 901 23rd Street, N.W., Washington, D.C.

Rx ANALYSIS

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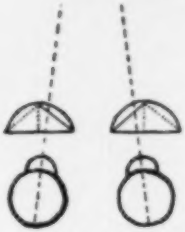

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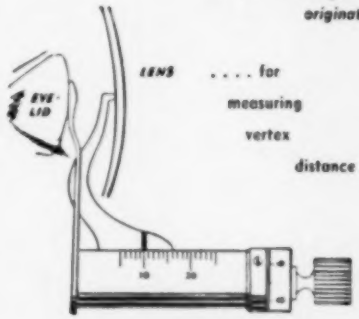

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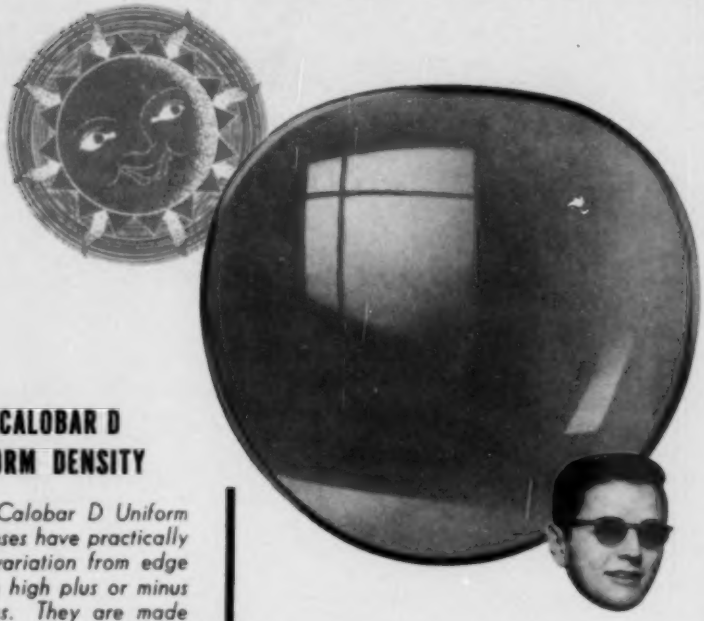

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